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(54) **Amino acid sequences of anti-idiotypic antibodies against anti-cancer human monoclonal antibody, and dna base sequences encoding those sequences**

(57) Amino acid sequences of the H chain and L chain variable regions of mouse monoclonal antibodies: Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 against idiotypes of a cancer cell antigen-specific human immunoglobulin CLN/IgG produced by a human/human fused cell strain CLN/SUZ H11, and base sequences of the genes of the variable regions are disclosed.

The above amino acid sequences and the base sequences are useful in medical and pharmaceutical fields such as prophylaxis, treatment and/or diagnosis of human diseases, and/or in pharmacological and/or biochemical fields, etc. such as biochemical reagents, and reagents for purification of biomacromolecules.

**EP 0 702 082 A1**

## Description

## Detailed Description of the Invention

5 This invention relates to the structure of the variable regions of mouse immunoglobulins against idiotypes of an antigen-specific human immunoglobulin, useful in wide fields, for example in pharmaceutical fields such as prophylaxis, treatment and/or diagnosis of human diseases, and/or in pharmacological and/or biochemical fields such as biochemical reagents and reagents for purification of biomacromolecules.

10 More detailedly, this invention relates to the amino acid sequences of the H chain and L chain variable regions of mouse immunoglobulins against idiotypes of a cancer cell antigen-specific human immunoglobulin produced by a human/human fused cell strain CLN/SUZ H11 from a B cell of a patient carrying human cervical carcinoma and a human lymphoblastoid cell strain, and relates to the base sequences of the genes of the variable regions.

15 Since the development of the technique of formation of monoclonal antibodies by cell fusion or immortalization of cells, many useful antibodies have been obtained using mainly mice. Among them, monoclonal antibodies against malignant tumor cells are utilized not only for fundamental researches such as analyses of tumor antigens, but in serum diagnoses, image diagnoses of tumors using labeled antibodies, and have extremely high utilization value. Particularly, human-derived anti-cancer monoclonal antibodies are expected as ideal antibodies in the clinical field, since they have only faint or no side effects.

20 In such circumstances, one of the present inventors, as disclosed detailedly in Japanese Laid-Open Patent Publication No. 201994/1983 (= U. S. Patent No. 5,286,647; EP-A-839,02157.3), Japanese Laid-Open Patent Publication No. 135898/1984 and Japanese Laid-Open Patent Publication No. 137497/1984, established a cell strain CLN/SUZ H11 (ATCC No. HB 8307) which produces a human monoclonal antibody having a high reactivity with human cancer cells. Interesting findings are obtained about the antibody (named CLN-IgG) produced by this cell strain, that the antibody class is IgG; the isotypes are  $\gamma 1$  type and  $\kappa$  type; and the antibody binds to a cancer antigen immunohistologically existing on the surface of the cancer cells and moreover inhibits proliferation of the cancer cells. At present, the whole amino acid sequence and DNA base sequence of the antibody are clarified (Japanese Laid-Open Patent Publication No. 346792/1992 = WO 92/20799).

25 On the other hand, since Jerne put forward the so-called network theory, various researches have been made on the structure of the variable regions of antibodies. An antibody binds to an antigen at its variable region (antigen combining site). Therefore, the variable regions of antibodies have various three-dimensional-like structures in accordance with the structures of the antigenic determinants on the surfaces of antigens to be recognized. Thus, an antibody itself can be considered to be an antigen, and in the case, the structures of the variable regions of the antibody are called idiotypes, and antibodies against the idiotypes of the antibody are called anti-idiotypic antibodies. The structure corresponding to an antigenic determinant is called an idiotope. An idiotype can be thought to be an aggregate of idiotypes. It was reported that among anti-idiotypic antibodies (Ab2) against an antibody (Ab1) exist antibodies which competitively inhibit binding of Ab1 to an antigen and have idiotopes analogous to antigens recognized by the antibodies, i.e. antibodies having structures as so-called internal images of the antigen.

30 In view of the above findings, anti-idiotypic antibodies are expected to be utilized for the purpose of treatment and/or diagnosis of cancers.

40 For example, as for the purpose of cancer treatment, a vaccine therapy using an anti-idiotypic antibody as an antigen is made possible. It is generally difficult to get cancer antigens in large amounts, and it is restricted from a safety aspect and an ethical aspect to directly immunize human beings with cancer cells as antigens. Therefore, these problems can be avoided by performing immunization with an anti-idiotypic antibody in place of an antigen.

45 In a diagnostic aspect, anti-idiotypic antibodies can be utilized to examine the state of immune reactions against cancer cells. Specifically, it serves for early detection of cancers, judgment of therapeutic effects to detect or determine one's antibodies against cancer antigens existing in the blood or humor of cancer patients.

Under such technical background, problems as stated below are underlying to be solved.

1) When anti-idiotypic antibodies are utilized as vaccines or diagnostic drugs, it is necessary to provide these antibodies in large amounts and stably. 2) There is a possibility to give more powerful vaccines or diagnostic drugs abounding in functionality by altering or modifying the antibodies.

50 A method by gene manipulation is considered as a means for solving the above problems, i.e. a means for realizing improvement of production amount of the antibodies and elevation or modification of the activities of the antibodies.

For example, in the case of the problem of 1), it can be considered to solve the problem by cloning such an antibody gene, introducing the gene into host cells such as animal cells or *Escherichia coli*, expressing the antibody gene to give a large amount of the antibody, and in the case of the problem of 2), it can be considered to alter such an antibody so as to have stronger immunogenicity by artificially changing the antibody gene, or to design an antibody molecule having a higher vaccinal activity by adding a function which the antibody does not inherently have, for example an enzymatic activity, an immunity induction activity or the like to the antibody molecule or a fragment thereof.

For accomplishment of these purposes, separation of anti-idiotypic antibody genes, and clarification of their structures are necessary. However, there has not so far been known anything at all about the structures of L chains and H chains constituting anti-idiotypic antibodies against idiotypes of CLN-IgG, and the gene structures of the variable regions having a function to specifically bind to idiotopes of CLN-IgG.

5 Thus the main object of this invention is to clarify the gene structures of the L chains and the H chains of anti-CLN-IgG idio type antibodies.

The present inventors have succeeded in creating hybridomas producing, respectively, five kinds of mouse anti-CLN-IgG idio type antibodies (Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33) having  $\gamma 1$  and  $\kappa$  isotypes against the idiotypes of CLN-IgG; have separated, from the hybridomas, cDNAs encoding the L chains and H chains of the anti-idiotypic  
10 antibodies, respectively; have clarified their DNA base sequences; have determined, based on these sequences, the amino acid sequences of the L chains and H chains of the antibodies, respectively; and have completed this invention.

Thus, according to this invention are provided an immunoglobulin H chain variable region fragment which contains a hypervariable region CDR1 having an amino acid sequence selected from

15

(1) Ser Tyr Trp Met His;  
Asp Tyr Tyr Met Asn; and  
Asn Tyr Trp Met Gln ,

20

a hypervariable region CDR2 having an amino acid sequence selected from

25

(2) Ala Ile Tyr Pro Gly Asn Ser  
Asp Ile Ser Tyr Ser Gln Asn  
Phe Lys Asp;  
Phe Ile Arg Asn Lys Ala  
30 Asn Leu Tyr Thr Thr Asp  
Tyr Ser Ala Ser Val Lys  
Gly;  
Phe Ile Arg Asn Lys Ala  
35 Asn Tyr Tyr Thr Thr Glu  
Tyr Ser Ala Ser Val Lys  
Gly; and  
40 Ala Ile Tyr Pro Gly Asp  
Gly Asp Thr Arg Tyr Thr  
Glu Lys Phe Lys Gly .

45

50

55

and a hypervariable region CDR3 having an amino acid sequence selected from

(3) Glu Glu Tyr Asp Tyr Asp  
 Thr Leu Asp Tyr;  
 Asp Arg Gly Gly Arg Asp  
 Trp Tyr Phe Asp Val;  
 Asp Gly Phe Leu Arg Asp  
 Trp Tyr Phe Asp Val; and  
 Ser Gly Tyr Tyr Gly Ser  
 Phe Val Gly Phe Ala Tyr;

and DNA and RNA fragments encoding the immunoglobulin H chain variable region fragment.

According to this invention are further provided an immunoglobulin L chain fragment which contains a hypervariable region CDR1 having an amino acid sequence selected from

(1) Tyr Arg Ala Ser Lys Ser Val  
 Gln Leu His Leu Ala Ile Val  
 Tyr Met His;  
 Tyr Arg Ala Ser Lys Ser Val  
 Ser Thr Ser Gly Tyr Ser Tyr  
 Met His;  
 Lys Ala Ser Gln Asp Val Asn  
 Thr Ala Val Ala; and  
 Lys Ala Ser Gln Asp Val Thr  
 Thr Asp Val Ala ,

a hypervariable region CDR2 having an amino acid sequence selected from

(2) Leu Val Ser Asn Leu Glu Ser;  
 Leu Val Ser Asn Leu Asp Ser; and  
 Ser Ala Ser Tyr Arg Tyr Thr ,

and a hypervariable region CDR3 having an amino acid sequence selected from

(3) Gln His Ile Arg Val Ala Tyr  
 Thr;  
 Gln His Ile Arg Gly Ala Tyr  
 Thr;  
 Gln His Ile Glu Gly Ala Tyr  
 Thr;  
 Gln Gln His Tyr Ser Pro Pro  
 Leu Thr; and  
 Gln Gln His Tyr Ser Thr Ala  
 Trp Thr;

and DNA and RNA fragments encoding the immunoglobulin L chain variable region fragment.

In this invention, cytoplasmic RNAs were prepared from the five mouse hybridomas, respectively; the RNAs were converted to cDNAs by a reverse transcriptase; the antibody genes were amplified using these cDNAs as templates and using the PCR method; the amplified DNA fragments were integrated into plasmids and cloned; the base sequences of the insertion DNAs of the plasmids purified from *Escherichia coli* clones isolated were determined, and the amino acid sequences were determined based on the base sequences. These steps are further detailedly described below.

#### [1] Isolation of cytoplasmic RNAs

Each mouse hybridoma is cultured and proliferated in a culture medium, e.g. and RDF or RPMI 1640 medium, containing 5% fetal bovine serum under a suitable condition, e.g. under a condition of 37°C and a carbon dioxide concentration of 5%; the resultant cells are collected by centrifugation; and the cytoplasmic RNA is extracted from the cells by a conventional method, e.g. a method disclosed in 7.12 of Molecular Cloning (2nd edition, edited by Sambrook et al., Cold Spring Harbor Laboratory Press 1989). The resultant cytoplasmic RNA can further be utilized as a template for cDNA synthesis. Specifically in this invention, the cytoplasmic RNAs were extracted from mouse hybridomas No. 3, No. 17, No. 20, No. 27 and No. 33, and provided for synthesis of cDNAs.

#### [2] Synthesis of cDNAs

Using a cytoplasmic RNA obtained in the step of [1] as a template, a single-strand DNA complementary to the mRNA is synthesized in the presence of dATP, dGTP, dTTP and dCTP using, as a primer, an oligo dT corresponding to a poly A, or a synthetic nucleotide having a random sequence, and a reverse transcriptase. In the specific operations in the invention, cDNAs were synthesized using the cytoplasmic RNAs obtained in the step of [1] as templates and a random hexamer as a primer, respectively, and provided for the step of amplification of the antibody genes.

#### [3] Amplification of antibody genes by PCR

PCR reaction is performed in the presence of dATP, dGTP, dTTP, dCTP and Taq polymerase using as a template a single-strand cDNA obtained in the step of [2] and as a primer a sequence of the antibody gene (e.g., a sequence encoding a constant region, a variable region or a leader region of the antibody gene) to amplify the antibody gene. Suitably in the invention, the antibody genes were amplified using as templates the single-strand cDNAs obtained in the step of [2] and using synthetic DNA oligomers corresponding to the sequences of the leader regions and variable regions of the L chains and H chains of the antibodies, respectively.

#### [4] Cloning of PCR-amplified DNA fragments

A PCR-amplified DNA fragment obtained in the step of [3] is, directly or after treatment with restriction enzyme(s), ligated into one of various vectors, for example plasmid vectors such as pUC 18, pCR1000 and pCR™, phage vectors such as M 13 phage, and phagemid vectors such as pUC 118 and pBluescript SK<sup>+</sup> to prepare a vector containing the insertion fragment. Then, *Escherichia coli* is transformed with the vector, and a colony of the *Escherichia coli* containing

the targeted antibody gene fragment is obtained. The purified vector recovered from the *Escherichia coli* is provided as a sample for determination of the DNA base sequence. In the specific operations in the invention, the PCR-amplified DNA fragments obtained in the step of [3] were directly ligated, respectively, into pCR1000 and pCR™ plasmid vector; an *Escherichia coli* INVαF' was transformed with each of the resultant plasmids; and the plasmids were purified from the resultant *Escherichia coli* colonies, respectively.

#### [5] Determination of the base sequences and amino acid sequences of the DNAs

The base sequence of the DNA at the insertion site in a plasmid obtained in the step of [4] can be determined using the Maxam-Gilbert method or the Sanger method. In the invention, the pCR1000 or pCR™ plasmid vectors containing the insertion fragments were purified, respectively; their base sequences were determined by the Sanger method; and the amino acid sequences were presumed based on their base sequences, respectively.

Hereafter, this invention is further specifically described below according to examples.

Drawings referred to in Examples are briefly described as follows.

Fig. 1 is a drawing showing isotypes of monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33.

Fig. 2 is a drawing showing the monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 specifically bind to CLN-IgG, and do not bind to other human IgGs.

Fig. 3 is a drawing showing that monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 are competitively inhibiting the binding between CLN-IgG and human matrical carcinoma cell ME-180.

Fig. 4 is a drawing where the amino acid sequences of the H chain variable regions of monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 are notated in parallel according to the Kabat's notation, and the regions of the hypervariable regions CDR1, CDR2 and CDR3 are determined.

Fig. 5 is a drawing where the amino acid sequences of the L chain variable regions of monoclonal antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 are notated in parallel according to the Kabat's notation, and the regions of the hypervariable regions CDR1, CDR2 and CDR3 are determined.

#### Example 1: Preparation of mouse hybridomas

100 µl of 1 mg/ml human IgG (produced by Cappel) is intraperitoneally injected to a Balb/c mouse on the first day after its birth to prepare a mouse having immunological tolerance to human IgG. Six weeks later, the mouse is immunized as follows with CLN-IgG as an antigen.

CLN-IgG purified from a culture medium of a human/human hybridoma CLN/SUZ H11 (ATCC No. HB8307) according to an ammonium sulfate precipitation method and protein A-affinity chromatography was adjusted to a concentration of 2 µg/µl with physiological saline; an equal amount of complete Freund's adjuvant solution was added; and after mixing and emulsification, 100 µl of the emulsion (corresponding to 100 µg of CLN-IgG) was subcutaneously injected into the immunologically tolerated mouse. Thereafter, similar immunization was repeated 4 to 5 times, the murine spleen was enucleated 4 days after the final immunization and made to be spleen cells, and they were used for the following cell fusion.

A mouse parent cells NS-1 (ATCC TIB 18) and the spleen cells are washed with portions of RPMI 1640 medium not containing serum, respectively, and the both of the cells are mixed and centrifuged. 1 ml of 50% polyethylene glycol (average molecular weight : 4,000) is added dropwise to the resultant precipitate over a period of 1 minute. 10 ml of RPMI 1640 medium is further added over a period of 3 minutes, the mixture is centrifuged at 400 x g for 5 minutes, the precipitate is suspended in 10 ml of RPMI 1640 medium containing 20% fetal bovine serum, and the suspension is spread into a 96-well microplate.

Thereafter, the cells were cultured in HAT medium for 14 to 21 days, transferred to HT medium, and finally cultured in RPMI 1640 medium containing 10% fetal bovine serum.

The antibody titers in the culture supernatants on the wells where proliferation was observed were assayed by an enzyme-labeled antibody technique; hybridoma clones secreting monoclonal antibodies which bind to CLN-IgG but not to human IgG were obtained from the appropriate wells by the limiting dilution method; and these hybridoma clones were named No. 3, No. 17, No. 20, No. 27 and No. 33.

#### Example 2: Determination of isotypes of the mouse antibodies

Isotypes of the antibodies secreted from the 5 mouse hybridomas obtained in Example 1 were determined as follows using a mouse monoclonal antibody isotyping kit (produced by Amersham Co.).

The mouse hybridomas are started to be cultured at a concentration each of  $5 \times 10^4$ /ml in portions of RPMI 1640 medium containing 10% fetal bovine serum, respectively, and 5 days later the culture supernatants are obtained, one stick portions of the typing sticks are placed in test tubes, respectively; 3 ml portions of the culture supernatants 5-fold diluted with TBS-T (Tris-buffered saline (TBS, pH 7.6) containing 0.1% Tween 20) are added thereto respectively; and



the mixtures are incubated at room temperature for 15 minutes. The culture supernatants are discarded, 5 ml portions of TBS-T are added, and the typing sticks are washed at room temperature for 5 minutes. TBS-T was discarded, and the washing was repeated once more. 3 ml portions of a peroxidase-labeled anti-mouse antibody 500-fold diluted with TBS-T are added, and the mixtures are incubated at room temperature for 15 minutes. The typing sticks are washed twice in the same manner as above; 3 ml portions of an enzyme substrate solution (obtained by adding one drop of 30% aqueous hydrogen peroxide to 50 ml of a TBS solution of 4-chloro-1-naphtol) are added; the mixtures are subjected to reaction at room temperature for 15 minutes; and then the sticks are washed with distilled water. The isotypes of the mouse antibodies are determined based on the resultant signals, respectively.

As a result, as shown in Fig. 1, all the isotypes of these antibodies were  $\gamma 1$  and  $\kappa$ .

#### Example 3: Examination of specificities of the anti-idiotypic antibodies

It was examined according to a dot blot technique, using an ECL Western blotting detecting reagent (produced by Amersham Co.), that the mouse anti-CLN-IgG idiotype antibodies specifically bind to CLN-IgG. The process is stated below.

CLN-IgG and human IgG1 (produced by Protogen Co.) were diluted with PBS to concentrations of 50 to 0.2  $\mu\text{l/ml}$ , respectively. 2  $\mu\text{l}$  portions of the thus prepared samples were spotted on a number of Hybond-ECL nitrocellulose membrane (produced by Amersham Co.), respectively and after being dried, the nitrocellulose membranes were allowed to stand at room temperature for one hour in PBS-T (0.3% Tween 20-containing PBS) containing 5% skim milk. After being washed with PBS-T, the nitrocellulose membranes were allowed to stand at room temperature for one hour in the culture supernatants (500-fold diluted with PBS-T) of mouse hybridomas No. 3, No. 17, No. 20, No. 27 and No. 33, respectively. After being washed with PBS-T, the nitrocellulose membranes were allowed to stand at room temperature for one hour in portions of a peroxidase-labeled sheep anti-mouse Ig antibody 3,000-fold diluted with PBS-T, respectively. After being washed with PBS-T, the nitrocellulose membranes were subjected to reaction for one minute in portions of the ECL detecting reagent, and sheets of X-ray film were exposed for 30 seconds to the light emitted from the resultant nitrocellulose membranes, respectively.

The results of the sheets of X-ray film developed are shown in Fig. 2. Any of the five antibodies bound to CLN-IgG, but did not bind to human IgG1. Namely, it was revealed that these antibodies are specific to CLN-IgG.

Next, it was examined whether or not the mouse antibodies have an activity to inhibit the binding of a human monoclonal antibody CLN-IgG to a human cancer cell. The method is stated below.

A human cervical carcinoma cell ME-180 (available from ATCC) is cultured in DF medium (a 1:1 mixed medium of DME : F-12) containing 10% fetal bovine serum. At the stage when the number of the cells becomes  $5 \times 10^6$  to  $1 \times 10^7$ , the cells are detached from the bottom face of the Petri dish using trypsin, collected by centrifugation and sufficiently washed with the medium. A constant number ( $10^5/100 \mu\text{l}$ ) each of the cells is placed in each well of a 96-well microtiter plate, and allowed to stand at 37°C overnight to be attached on the plate. 50  $\mu\text{l}$  portions of 3% glutaraldehyde solution were added dropwise into the respective wells, and the mixtures are allowed to stand at 37°C for 20 minutes to fix the cells. The cells of each well are centrifuged at 200 x g for 10 minutes and washed three times with a gelatin buffer (10 mM phosphate-buffered physiological saline containing 0.3% gelatin); 200  $\mu\text{l}$  portions of 1% bovine serum albumin (BSA) solution are added dropwise; and the mixture is allowed to stand at 37°C for one hour to block the plate. The cells are washed three times with the gelatin buffer to remove BSA not adsorbed. Thereafter, dilutions at various rates (100 to 1,000,000-fold) of the ascites obtained by intraperitoneally inoculating into mice the various hybridomas secreting the mouse anti-idiotypic antibodies are added dropwise together with CLN-IgG (50  $\mu\text{g}$  each), and the mixtures are subjected to reaction at 37°C for one hour. The cells of these wells are washed three times with the gelatin buffer, 50  $\mu\text{l}$  portions of a 3,000-fold diluted peroxidase-conjugated goat anti-human Ig antibody (produced by TACO Co.) are added dropwise, respectively, and the mixtures are subjected to reaction at 37°C for 30 minutes. The cells are washed three times with the gelatin buffer, and portions of a substrate solution containing hydrogen peroxide and o-phenylenediamine are added to perform reaction in a darkroom. 10 minutes later, 50  $\mu\text{l}$  portions of 5N sulfuric acid are added to stop the reaction. When the peroxidase-conjugated goat anti-Ig antibody remains on the microplate, namely when the human IgG to be bound thereto remains, a yellow reaction product having absorption at 490 nm is formed. The amount of CLN-IgG bound to the cancer cell is determined by measuring the amount of the reaction product by a spectrometer.

It was clarified, according to the above method, that all the mouse antibodies Idio 3, Idio 17, Idio 20, Idio 27 and Idio 33 inhibit the binding of CLN-IgG to the cancer cell (Fig. 3).

From the foregoing, these mouse antibodies are antibodies against the idiotypes of CLN-IgG.

#### Example 4: Preparation of RNA

From the five kinds of mouse hybridomas No. 3, No. 17, No. 20, No. 27 and No. 33, the cytoplasmic RNAs were extracted according to the method disclosed in Molecular Cloning (2nd edition, edited by Sambrook et al., Cold Spring Harbor Laboratory Press 1989) 7, 12, as stated below.

10<sup>8</sup> each of the hybridomas cells are collected by centrifugation, and washed twice with 10 times each precipitate's volume of a phosphate-buffered saline. The cells of these groups are centrifuged at 2,000 x g and 4°C for 5 minutes, and the resultant precipitates are suspended in 200 µl portions of an RNA extracting solution (0.14 M NaCl, 1.5 mM MgCl<sub>2</sub>, 10 mM Tris-HCl pH 8.6, 0.5% Nonidet P-40, 1 mM dithiothreitol, 20 mM vanadylribonucleoside complex), respectively. The suspensions are subjected to vortex for 15 seconds and allowed to stand on ice for 5 minutes. The resultant suspensions are centrifuged at 12,000 x g for 30 seconds to remove the cell nuclei as precipitates; to the supernatants are, respectively, added 200 µl portions of a proteinase buffer (0.2 M Tris-HCl pH 8.0, 25 mM EDTA pH 8.0, 0.3 M NaCl, 1.2% SDS) and 1 µl portions of an aqueous proteinase K solution (20 mg/ml); and the mixtures are sufficiently stirred and subjected to incubation at 37°C for 30 minutes. Equal volume portions of phenol/chloroform are added to the reaction solutions, respectively, and the mixtures are stirred, centrifuged at 5,000 x g and room temperature for 10 minutes, and then allowed to separate into organic layers and aqueous layers, respectively. 400 µl portions of isopropanol cooled on ice in advance are added to the aqueous layers recovered, respectively, and the mixtures are allowed to stand on ice for 30 minutes. The mixtures are centrifuged at 12,000 x g and 4°C for 10 minutes to collect RNAs. The resultant RNA precipitates are washed with 1 ml portions of ethanol, dried under reduced pressure and suspended in appropriate amount portions of TE buffer, respectively. Using the cytoplasmic RNAs obtained according to the above operations, the antibody genes are amplified.

#### Example 5: Amplification and cloning of the antibody genes by the RT-PCR method

The antibody genes were amplified from the cytoplasmic RNAs obtained in Example 4, using a GeneAmp® RNA PCR kit (produced by Takara Shuzo Co., Ltd.). First, 20 µl each of reactive solutions were prepared containing PCR buffer II (x1), 5 mM MgCl<sub>2</sub>, 1 mM dATP, 1 mM dGTP, 1 mM dTTP and 1 mM dCTP, 1 U/µl an RNase inhibitor, 2.5 µM a random hexamer, 2.5 U/µl a reverse transcriptase and 100 ng each of the above-mentioned cytoplasmic RNAs, respectively; 20 µl portions of a mineral oil were overlaid thereon respectively; and incubations were performed at room temperature for 10 minutes, at 42°C for 15 minutes, at 99°C for 5 minutes and then at 4°C for 5 minutes to perform cDNA synthesis by reverse transcription reaction. Then, 80 µl portions of a solution consisting of 4 µl of 25 mM MgCl<sub>2</sub>, 8 µl of 10x PCR buffer II, 65.5 µl of sterile distilled water, 0.5 µl of AmpliTaq DNA polymerase (5 U/µl) and 2 µl of PCR primers (each 100 pmoles) were added to the above 20 µl of the reverse transcription reaction solutions; 80 µl portions of the mineral oil were overlaid thereon; and PCR reactions were successfully performed. Each reaction was performed by repeating 30 times the cycle of 94°C for 1.5 minutes, 50°C for 2 minutes and then 72°C for 3 minutes. The base sequences of the PCR primers are shown below. The primers contained in a Ig-Prime™ kit (produced by Novagen Co.) were used except for the primer of the leader sequence C for H chains.

Primer for H chains	
Leader sequence A	5' GGGAATTCATGRASSTSKGGYTMACTKGRTTT 3'
Leader sequence B	5' GGGAATTCATGRAATGSASCTGGGTWYTYCTCTT 3'
Leader sequence C	5' TTAAATGGTATCCAGTGT 3'
Constant region	5' CCCAAGCTTCCAGGGRCCARKGGATACIGRTGG 3'

Primer for L chains	
Leader sequence A	5' GGGAATTCATGRAGWCACAKWCYCAGGTCTTT 3'
Leader sequence B	5' GGGAATTCATGGAGACAGACACACTCCTGCTAT 3'
Constant region	5' CCCAAGCTTACTGGATGGTGGGAAGATGGA 3'

In the above, the alphabets other than A, G, C and T mean the following bases. R=A/G, W=A/T, I=inosine, Y=C/T, D=A/G/T, K=G/T, H=A/C/T, S=C/G, V=A/C/G, M=A/C, B=G/C/T

10 µl portions of the resultant 100 µl each of the PCR reaction products are subjected to 1.5% agarose gel electrophoresis, and it was confirmed that the antibody gene fragments each about 600 bp long were amplified. As a result, in the case of the H chains, the antibody genes derived from No. 3 and No. 17 were amplified in the leader sequence A,

the antibody genes derived from No. 20 and No. 27 were amplified in the leader sequence B, and the antibody gene derived from No. 33 was amplified in the leader sequence C. On the other hand, in the L chains, the antibody genes derived from No. 27 and No. 33 were amplified in the case where the leader sequence A was used, and the antibody genes derived from No. 3, No. 17 and No. 20 were amplified in the leader sequence B.

5 Each of the PCR-amplified fragments about 600 bp long was integrated into pCR 1000 vector or pCR™ vector using TA cloning kit (produced by Invitrogen Co.). Specifically, ligation mix solutions were prepared by mixing 1 µl portions of the PCR reaction products, 1 µl portions of 10 x the ligation buffer, 2 µl portions of pCR1000 or pCR™ vector (corresponding to 50 µg), 1 µl of T4 DNA ligase and 6 µl portions of sterilized water, respectively; and incubated overnight at 12°C. Separately, 50 µl portions of a suspension of a competent *Escherichia coli* INVαT strain, to which portions were  
10 added 2 µl portions of 0.5 M β-mercaptoethanol, respectively, were prepared; and 1 µl portions of the above ligation mix solutions are added thereto, respectively. The mixtures are allowed to stand on ice for 30 minutes, incubated at 42°C for one minute, and rapidly cooled on ice for 2 minutes. 450 µl portions of SOC medium warmed to 42°C in advance were added to the resultant *Escherichia coli* solutions, respectively, and the mixtures are cultured with shaking at 37°C for one hour. Meanwhile, 25 µl portions of X-Gal (40 mg/µl) are spreaded onto a number of LB agar plates each containing  
15 Kanamycin (50 µg/ml), respectively, and the agar plates are incubated at 37°C until each X-Gal completely permeates the agar plate.

200 µl portions of the *Escherichia coli* culture broths after completion of culture were spread on the agar plate dried, respectively, and the plates were allowed to stand at 37°C overnight to give white colonies each having Kanamycin resistance.

20 Plasmids were purified from the *Escherichia coli* clones containing the respective antibody genes, and named 3KB11, 17KB1, 20KB1, 27KA2, 33KA26, 3GB1, 17GB7, 20GA2, 27GA5 and 33GC003, respectively. Purification of the plasmids is performed as follows.

The *Escherichia coli* strains containing the above plasmids, respectively, are cultured 37°C overnight in 100 ml portions of LB medium containing Kanamycin (50 µg/ml), respectively. Each of the resultant culture broths is centrifuged  
25 at 3,000 rpm for 10 minutes; the cells collected are suspended in 3 ml of an ice-cooled suspension (50 mM glucose, 10 mM EDTA, 2 mM Tris-HCl pH 8.0); and the suspension is allowed to stand at room temperature for 5 minutes. 6 ml of an alkali lysing solution (0.2 N sodium hydroxide, 1% SDS) is added, and the mixture is mixed by gently turning the centrifugation vessel upside down, and allowed to stand on ice for 5 minutes. 4.5 ml of an ice-cooled neutralizing solution (5 M potassium acetate pH 4.8) is added, and the mixture is centrifuged at 12,000 rpm and 4°C for 10 minutes. The  
30 supernatant is transferred into another centrifugation vessel; 1 ml of heat-treated 100 µg/ml RNase A solution is added; and the mixture is subjected to reaction for one hour in an incubator of 37°C to perform RNA digestion. To the reaction solution are added 6 ml of TE buffer-saturated phenol and 6 ml of chloroform/isoamyl alcohol (24:1), and the mixture is subjected to vortex for 30 seconds and then centrifuged at 10,000 rpm and 4°C for 3 minutes. The aqueous layer is transferred into another centrifugation vessel, an equal amount of isopropanol is added, and the mixture is sufficiently  
35 mixed and then centrifuged at 10,000 rpm and room temperature for 10 minutes.

The resultant precipitate is washed with 1 ml of 70% cold (-20°C) ethanol, dried under reduced pressure, and dissolved in 480 µl of sterilized water. The solution is transferred into an Eppendorf tube; 120 µl of 4 M NaCl and 600 µl of 13% polyethylene glycol #6000 are added; and the mixture is allowed to stand on ice for 20 minutes. The mixture is then centrifuged at 10,000 rpm and 4°C for 10 minutes, and the precipitate is washed with 1 ml of 70% cold (-20°C) ethanol,  
40 dried under reduced pressure and dissolved in 100 µl of TE buffer. The resultant purified plasmid was used as a template for sequencing reaction.

#### Example 6: Determination of the base sequences

45 Sanger reactions were performed using as templates the plasmids cloning purified in Example 5 and a fluorescence-labeled primer; the reaction products were analyzed by a DNA sequencer DSQ-1 (produced by Shimadzu Corporation); and the DNA base sequences of the insert parts of the plasmids were also determined.

The sequencing reactions were performed using AmpliTaq cycle sequencing kit (produced by Takara Shuzo Co., Ltd.) and a fluorescence-labeled primer in a reagent kit (produced by Wakunaga Pharmaceutical Co., Ltd.) exclusively  
50 used for a fluorescence-type DNA sequencer. First, 2 to 4 µg of one of the plasmids purified as stated in Example 5 is mixed with 1 µl of the FITC-labeled primer (1 p mole/µl, forward or reverse is used) and 2 µl of the 10 x cycling mix solution, and sterilized water is added to prepare 10 µl in final volume of a reaction mix. Four tubes are prepared in which 2 µl portions of the termination mix (A, G, C, T) were placed in advance, respectively. 2 µl portions of the above reaction mix were taken and placed into the respective tubes. The mixtures are corrected by centrifugation, 10 µl portions  
55 of a mineral oil are overlaid, and cycling reactions are performed under the following conditions; Precycle 95°C, 3 minutes; first cycle 95°C 30 seconds, 60°C 30 seconds, 72°C 1 minute (repeated 15 times); second cycle 95°C 30 seconds, 72°C 1 minute (repeated 15 times); postcycle 4°C.

2 µl portions of a reaction-stopping dye solution (95% formaldehyde, 20 mM EDTA, 0.05% methyl violet) are added, and the mixtures are mixed by centrifugation and preserved at 20°C until they are electrophoresed.

As 5% polyacrylamide gel was used one obtained by adding pure water to 30 g of urea, 6 ml of 10 x TBE buffer (0.89 M Tris-HCl, 0.89 M boric acid, 0.025 M EDTA disodium salt) and 10 ml of 30% acrylamide solution (28.5% acrylamide and 1.5% methylenebisacrylamide, both produced by BIO-RAD Co.) to make the whole volume 60 ml; filtering the mixture with 0.22- $\mu$ m filter; deaerating the filtrate for 30 minutes; adding 150  $\mu$ l of 10% ammonium persulfate and 15  $\mu$ l of TEMEO; allowing the mixture to stand overnight to make it gel.

The gel was set in the DNA sequencer DSQ-1, and prerun was performed at a constant voltage of 1,000 V for one hour. Each of the samples was denatured at 95°C for 3 minutes immediately before electrophoresis, and rapidly cooled on ice, and 2 to 3  $\mu$ l of the reaction solution was sucked up from the bottom part of the tube by a micro-syringe and loaded onto the gel. Samples run was performed at a constant electric power of 20 W for 12 hours.

After completion of electrophoresis, the base sequence was determined using the software attached to DSQ-1. The sequence was confirmed by sequencing both of the sense and antisense chains of the same plasmid from both directions.

The resultant base sequences of the variable regions of the H chains and L chains of the five kinds of the mouse monoclonal antibodies, and amino acid sequences presumed therefrom are shown in the following sequence listing. Relation between the sequence numbers and the sequences of the clones are as follows:

- Sequence No. 1 : Idio 3 H chain variable region (clone 3GB1)
- Sequence No. 2 : Idio 17 H chain variable region (clone 17GB7)
- Sequence No. 3 : Idio 20 H chain variable region (clone 20GA2)
- Sequence No. 4 : Idio 27 H chain variable region (clone 27GA5)
- Sequence No. 5 : Idio 33 H chain variable region (clone 33GC003)
- Sequence No. 6 : Idio 3 L chain variable region (clone 3KB11)
- Sequence No. 7 : Idio 17 L chain variable region (clone 17KB1)
- Sequence No. 8 : Idio 20 L chain variable region (clone 20KB1)
- Sequence No. 9 : Idio 27 L chain variable region (clone 27KA2)
- Sequence No. 10 : Idio 33 L chain variable region (clone 33KA26)

#### Example 7 Determination of hypervariable regions

The amino acid sequences obtained in Example 6 were notated in parallel according to the numbering of Kabat et al.'s data base (Sequences of proteins of immunological interest Fifth edition, U. S. Department of health and human services, Public health service, National Institutes of Health, NIH Publication No. 91-3242, Kabat et al. 1991), and the amino acid sequences of the hypervariable regions CDR1, CDR2 and CDR3 of each antibody were identified (Fig. 4, H chains, Fig. 5 L chains). In order to confirm the novelty of the identified amino acid sequences of the hypervariable regions CDR1, CDR2 and CDR3, retrieval by a computer was performed using the above Kabat et al.'s data base and a protein data base NBRF-PDB (National Biomedical Research Foundation - protein data base) Release 36.

As a result, the amino acid sequences of Idio 3 H chain CDR1, Idio 17 H chain CDR1, Idio 20 H chain CDR1, Idio 27 H chain CDR1, Idio 33 H chain CDR2, Idio 3 L chain CDR2, Idio 17 L chain CDR2, Idio 27 L chain CDR2 and Idio 33 L chain CDR2 were the same as those of known antibodies, but the amino acid sequences of other CDRs were

revealed to be novel sequences.

# Sequence Listing

Seq. I.D. number : 1

Sequence length : 399

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..399

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..27

Characteristics determination method : S

## Sequence

CTG TCG GTA ACT TCA GGG GTC TAC TCA GAG GTT CAG CTC CAG CAG TCT	48
Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln Gln Ser	
-5 1 5	
GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC AAG	96
Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys Lys	
10 15 20	
GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA CAG	144
Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys Gln	
25 30 35	
AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA AAT	192
Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn	
40 45 50 55	
AGT GAT ATT AGC TAC AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG ACT	240
Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu Thr	
60 65 70	
GCC GTC ACA TCC ACC AGC ACT GCC TAC ATG GAA CTC AGA AGC CTG ACA	288
Ala Val Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr	
75 80 85	
AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT TAC	336
Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asp Tyr	
90 95 100	
GAC ACC CTG GAC TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TCC TCA	384
Asp Thr Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser	
105 110 115	
GCC AAA ACG ACA CCC	399
Ala Lys Thr Thr Pro	
120	

## Sequence Listing

Seq. I.D. number : 2

Sequence length : 402

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..402

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..30

Characteristics determination method : S

## Sequence

ATT CTG TCG GTA ACT TCA GGG GTC TAC TCA GAG GTT CAG CTC CAG CAG	48
Ile Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln Gln	
-10 -5 1 5	
TCT GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC	96
Ser Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys	
10. 15 20	
AAG GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA	144
Lys Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys	
25 30 35	
CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA	192
Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly	
40 45 50	
AAT AGT GAT ATT AGC TAC AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG	240
Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu	
55 60 65	
ACT GCC GTC ACA TCC ACC AGC ACT GCC TAC ATG GAA CTC AGA AGC CTG	288
Thr Ala Val Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu	
70 75 80 85	
ACA AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT	336
Thr Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asp	
90 95 100	
TAC GAC ACC CTG GAC TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TCC	384
Tyr Asp Thr Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser	
105 110 115	
TCA GCC AAA ACG ACA CCC	402
Ser Ala Lys Thr Thr Pro	
120	

## Sequence Listing

Seq. I.D. number : 3

Sequence length : 438

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..438

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..57

Characteristics determination method : S

## Sequence

ATG GAG TTC GGG CTA AAC TGG GTT TTC CTT GTA ACA CTT TTA AAT GGT	48
Met Glu Phe Gly Leu Asn Trp Val Phe Leu Val Thr Leu Leu Asn Gly	
-15 -10 -5	
ATC CAG TGT GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG	96
Ile Gln Cys Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Gln	
1 5 10	
CCT GGG GGT TCT CTC AGA CTC TCC TGT GCA ACT TCT GGG TTA ACC TTC	144
Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Leu Thr Phe	
15 20 25	
ACT GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GAA CTT	192
Thr Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Glu Leu	
30 35 40	
GAA TGG TTG GGT TTT ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA GAC	240
Glu Trp Leu Gly Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr Asp	
45 50 55 60	
TAC AGT GCA TCT GTG AAG GGT CGG TTC ACC ATC TCC AGA GAT AAT CCC	288
Tyr Ser Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Pro	
65 70 75	
CAA AGC ATC CTC TAT CTT CAA ATG AAC ACC CTG ACA ACT GAG GAC AGT	336
Gln Ser Ile Leu Tyr Leu Gln Met Asn Thr Leu Thr Thr Glu Asp Ser	
80 85 90	
GCC ACT TAT TAC TGT GCA AGA GAT AGG GGG GGG AGG GAC TGG TAC TTC	384
Ala Thr Tyr Tyr Cys Ala Arg Asp Arg Gly Gly Arg Asp Trp Tyr Phe	
95 100 105	
GAT GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA GCC AAA ACG	432
Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys Thr	
110 115 120	
ACA CCC	438
Thr Pro	
125	

## Sequence Listing

Seq. I.D. number : 4

Sequence length : 411

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..411

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..30

Characteristics determination method : S

## Sequence

```

25      CTT GTA ACA CGT TTA AAT GGT ATC CAG TGT GAG GTG AAG CTG GTG GAG      48
      Leu Val Thr Arg Leu Asn Gly Ile Gln Cys Glu Val Lys Leu Val Glu
      -10          -5          1          5
      TCT GGA GGA GGC TTG GTA CAG CCT GGG GGT TCT CTG AGA CTC TCC TGT      96
      Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys
      10          15          20
      GCA ACT TCT GGG TTC ACC TTC ACT GAT TAC TAC ATG AAC TGG GTC CGC      144
      Ala Thr Ser Gly Phe Thr Phe Thr Asp Tyr Tyr Met Asn Trp Val Arg
      25          30          35
      CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG GGT TTT ATT AGA AAC AAA      192
      Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu Gly Phe Ile Arg Asn Lys
      40          45          50
      GCT AAT TAT TAC ACA ACA GAG TAC AGT GCA TCT GTG AAG GGT CGG TTC      240
      Ala Asn Tyr Tyr Thr Thr Glu Tyr Ser Ala Ser Val Lys Gly Arg Phe
      55          60          65
      ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC CTC TAT CTT CAA ATG AAC      288
      Thr Ile Ser Arg Asp Asn Ser Gln Ser Ile Leu Tyr Leu Gln Met Asn
      70          75          80          85
      ACC CTG AGA GCT GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA GAT GGG      336
      Thr Leu Arg Ala Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg Asp Gly
      90          95          100
      TTC CTA CGG GAC TGG TAC TTC GAT GTC TGG GGC GCA GGG ACC ACG GTC      384
      Phe Leu Arg Asp Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val
      105          110          115
      ACC GTC TCC TCA GCC AAA ACG ACA CCC      411
      Thr Val Ser Ser Ala Lys Thr Thr Pro
      120          125

```



## Sequence Listing

Seq. I.D. number : 5

Sequence length : 363

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..363

Characteristics determination method : S

## Sequence

25	GAG GTT CAG CTC CAG CAG TCT GGG GCT GAA CTG GCA AGA CCT GGG GCT	48
	Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala	
	1 5 10 15	
	TCA GTG AAC TTG TCC TGC AAG GCT TCT GGC TAC ACC TTT ACT AAC TAC	96
	Ser Val Asn Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr	
30	20 25 30	
	TGG ATG CAG TGG GTA AAA CAG AGG CGT GGA CAG GGT CTG GAA TGG ATT	144
	Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile	
	35 40 45	
35	GGG GCT ATT TAT CCT GGA GAT GGT GAT ACT AGG TAC ACT CAG AAG TTC	192
	Gly Ala Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr Thr Gln Lys Phe	
	50 55 60	
	AAG GGC AAG GCC ACA TTG ACT GCA GCT AAA TCC TCC AGC ACA GCC TAC	240
40	Lys Gly Lys Ala Thr Leu Thr Ala Ala Lys Ser Ser Ser Thr Ala Tyr	
	65 70 75	
	ATG CAA CTC AGC AGC TTG GCA TCT GAG GAC TCT GCG GTC TAT TAC TGT	288
	Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys	
45	80 85 90 95	
	GCA AGA TCG GGC TAC TAT GGT AGC TTC GTT GGG TTT GCT TAC TGG GGC	336
	Ala Arg Ser Gly Tyr Tyr Gly Ser Phe Val Gly Phe Ala Tyr Trp Gly	
	100 105 110	
50	CAA GGG ACT CTG GTC ACT GTC TCT GCA	363
	Gln Gly Thr Leu Val Thr Val Ser Ala	
	115 120	

## Sequence Listing

Seq. I.D. number : 6

Sequence length : 354

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..354

Characteristics determination method : S

## Sequence

25	GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CCT CTG	48
	Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Pro Leu	
	1 5 10 15	
	GGG CAG AGG GCC ACC ATC TCA TAC AGG GCC AGC AAA AGT GTG CAG TTA	96
	Gly Gln Arg Ala Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Gln Leu	
30	20 25 30	
	CAT CTG GCT ATA GTT TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG	144
	His Leu Ala Ile Val Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln	
	35 40 45	
35	CCA CCC AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC	192
	Pro Pro Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val	
	50 55 60	
	CCT GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC	240
40	Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn	
	65 70 75	
	ATC CAT CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC	288
	Ile His Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His	
	80 85 90 95	
45	ATT AGG GTA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA	336
	Ile Arg Val Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys	
	100 105 110	
	CGG GCT GAT GCT GCA CCA	354
50	Arg Ala Asp Ala Ala Pro	
	115	

## Sequence Listing

Seq. I.D. number : 7

Sequence length : 438

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..438

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..39

Characteristics determination method : S

## Sequence

25	CTA TGG GTA CTG CTG CTC TGG GTT CCA GGT TCC ACT GGT GAC ATT GTG	48
	Leu Trp Val Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Ile Val	
	-10 -5 1	
	CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG CAG AGG GCC	96
	Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala	
30	5 10 15	
	TCC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAT AGT	144
	Ser Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser	
	20 25 30	
	TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG CCA CCC AGA CTC CTC	192
35	Tyr Met His Trp Asn Gln Lys Pro Gly Gln Pro Pro Arg Leu Leu	
	35 40 45 50	
	ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC CCT GCC AGG TTC AGT	240
	Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val Pro Ala Arg Phe Ser	
	55 60 65	
40	GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG	288
	Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu	
	70 75 80	
	GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT AGG GGA GCT TAC	336
	Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Arg Gly Ala Tyr	
45	85 90 95	
	ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA CGG GCT GAT GCT GCA	384
	Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala Ala	
	100 105 110	
	CCA ACT GTA TCC ATC TTC CCA CCA TCC AGT AAG CTT GGG AAA CGG TTC	432
50	Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Lys Leu Gly Lys Arg Phe	
	115 120 125 130	
	GCA CCG	438
	Ala Pro	

## Sequence Listing

Seq. I.D. number : 8

Sequence length : 417

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 28..417

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 28..90

Characteristics determination method : S

## Sequence

```

25      GGCCGCG GTGAGAACCG TTGGGAATTC ATG GAG ACA GAC ACA CTC CTG      48
                                         Met Glu Thr Asp Thr Leu Leu
                                         -20          -15

30      CTA TGG GTA CTG CTG CTC TGG GTT CCA GGT TCC ACT GGT GAC ATT GTG      96
Leu Trp Val Leu Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Ile Val
          -10          -5          1

      CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG CAG AGG GCC      144
Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala
          5          10          15

35      ACC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAT AGT      192
Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser
          20          25          30

      TAT ATG CAC TGG AAC CAA CAG AGA CCA GGA CAG CCA CCC AGA CTC CTC      240
Tyr Met His Trp Asn Gln Gln Arg Pro Gly Gln Pro Pro Arg Leu Leu
          35          40          45          50

40      ATC TAT CTT GTA TCC AAC CTA GAC TCT GGG GTC CCT GCC AGG TTC AGT      288
Ile Tyr Leu Val Ser Asn Leu Asp Ser Gly Val Pro Ala Arg Phe Ser
          55          60          65

      GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG      336
Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu
          70          75          80

      GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT GAG GGA GCT TAC      384
Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Glu Gly Ala Tyr
          85          90          95

50      ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA      417
Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
          100          105

```

## Sequence Listing

Seq. I.D. number : 9

Sequence length : 420

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 31..420

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 31..90

Characteristics determination method : S

## Sequence

25	GCGGCCGCGG TGAGAACCGT TTGGGAATTC ATG GAG ACA CAG TCC CAG	48
	Met Glu Thr Gln Ser Gln	
	-20 -15	
	GTC TTT GTA TTC GTG TTT CTC TGG TTG TCT GGT GTT GAC GGA GAC ATT	96
	Val Phe Val Phe Val Phe Leu Trp Leu Ser Gly Val Asp Gly Asp Ile	
30	-10 -5 1	
	GTC ATG ACC CAG TCT CAC AAA TTC ATG TCC ACA TCA GTA GGA GAC AGG	144
	Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly Asp Arg	
	5 10 15	
35	GTC AGT ATC ACC TGC AAG GCC AGT CAG GAT GTG AAT ACT GCT GTA GCC	192
	Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala Val Ala	
	20 25 30	
	TGG TAT CAA CAG AAA CCA GGA CAA TCT CCT AAA CTA CTG CTT TAC TCG	240
	Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Leu Tyr Ser	
40	35 40 45	
	GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT CAC TTC ACT GGC AGT GGA	288
	Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp His Phe Thr Gly Ser Gly	
	50 55 60 65	
45	TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC GGT GTG CAG GCT GAA GAC	336
	Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Gly Val Gln Ala Glu Asp	
	70 75 80	
	CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT AGT CCT CCT CTC ACG TTC	384
	Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Pro Pro Leu Thr Phe	
	85 90 95	
50	GGT GCT GGG ACC AAG CTG GAA CTG AAA CGG GCT GAT	420
	Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala Asp	
	100 105	

55

## Sequence Listing

Seq. I.D. number : 10

Sequence length : 360

Sequence type : nucleic acid

Strandedness : double

Topology : linear

Sequence kind : mRNA

Original source

Organism : mouse

## Sequence characteristics

Symbol expressing characteristics : CDS

Presence position : 1..360

Characteristics determination method : S

Symbol expressing characteristics : sig peptide

Presence position : 1..12

Characteristics determination method : S

## Sequence

GGT GTT GAC GGA GAC ATT GTG ATG ACA CAG TCT CAC AAA TTC ATG TCC	48
Gly Val Asp Gly Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser	
1 5 10	
ACA TCA GTT GGA GAC AGG GTC ACC ATC ACC TGC AAG GCC AGT CAG GAT	96
Thr Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp	
15 20 25	
GTG ACT ACT GAT GTA GCC TGG TAT CAA CAG AAA CCA CGA CAA TCT CCT	144
Val Thr Thr Asp Val Ala Trp Tyr Gln Gln Lys Pro Arg Gln Ser Pro	
30 35 40	
AAA CTA CTG ATT TAC TCG GCA TCC TAT CGG TAC ACT GGA GTC CCT GAT	192
Lys Leu Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp	
45 50 55	
CGC TTC ACT GGC AGT GGA TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC	240
Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser	
60 65 70 75	
AGT GTG CAG GCT GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT	288
Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr	
80 85 90	
AGT ACT GCG TGG ACG TTC GGT GGT GGC ACC AAG CTG GAA ATC AAA CGG	336
Ser Thr Ala Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg	
95 100 105	
GCT GAT GCT GCA CCA ACT GTA TCC	360
Ala Asp Ala Ala Pro Thr Val Ser	
110 115	

## SEQUENCE LISTING

5

## (1) GENERAL INFORMATION:

## (i) APPLICANT:

10

- (A) NAME:HAGIWARA, Yoshihide
- (B) STREET:4-14, Hiraisanso
- (C) CITY:Takarazuka-shi
- (D) STATE:Hyogo-ken
- (E) COUNTRY:Japan
- (F) POSTAL CODE (ZIP):none

15

(ii) TITLE OF INVENTION:AMINO ACID SEQUENCES OF ANTI-IDIOTYPIC ANTIBODIES AGAINST ANTI-CANCER HUMAN MONOCLONAL ANTIBODY, AND DNA BASE SEQUENCES ENCODING THOSE SEQUENCES

20

(iii) NUMBER OF SEQUENCES:48

## (iv) COMPUTER READABLE FORM:

25

- (A) MEDIUM TYPE:Floppy disk
- (B) COMPUTER:IBM PC compatible
- (C) OPERATING SYSTEM:MS DOS 4.0
- (D) SOFTWARE:Microsoft Word, Version 5.5

## (v) CURRENT APPLICATION DATA:

- (A) APPLICATION NUMBER:EP 94 115 683.8
- (B) FILING DATE:October 5, 1994

30

## (2) INFORMATION FOR SEQ ID NO: 1:

## (i) SEQUENCE CHARACTERISTICS:

35

- (A) LENGTH:5 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

## (ix) FEATURE:

- (A) NAME/KEY:H-CDR1-1
- (D) OTHER INFORMATION:hypervariable region

40

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:1:

Ser Tyr Trp Met His

5

45

## (2) INFORMATION FOR SEQ ID NO: 2:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:5 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

50

(ii) MOLECULE TYPE:protein

## (ix) FEATURE:

- (A) NAME/KEY:H-CDR1-2
- (D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 2:

55

Asp Tyr Tyr Met Asn

5

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:5 amino acids

(B) TYPE:amino acid

(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

(A) NAME/KEY:H-CDR1-3

(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:3:

Asn Tyr Trp Met Gln

5

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:17 amino acids

(B) TYPE:amino acid

(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

(A) NAME/KEY:H-CDR2-1

(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 4:

Ala Ile Tyr Pro Gly Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys

5

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15

Asp

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:19 amino acids

(B) TYPE:amino acid

(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

(A) NAME/KEY:H-CDR2-2

(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:5:

Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr Asp Tyr Ser Ala Ser

5

10

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Val Lys Gly

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:19 amino acids

(B) TYPE:amino acid

(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:



- (A) NAME/KEY:H-CDR2-3
- (D) OTHER INFORMATION:hypervariable region

5

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 6:

Phe Ile Arg Asn Lys Ala Asn Tyr Tyr Thr Thr Glu Tyr Ser Ala Ser  
                                   5                                  10                                  15  
 Val Lys Gly

10

(2) INFORMATION FOR SEQ ID NO: 7:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH:17 amino acids
  - (B) TYPE:amino acid
  - (D) TOPOLOGY:linear.

15

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:H-CDR2-4
- (D) OTHER INFORMATION:hypervariable region

20

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:7:

Ala Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr Thr Glu Lys Phe Lys  
                                   5                                  10                                  15  
 Gly

25

(2) INFORMATION FOR SEQ ID NO: 8:

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH:10 amino acids
  - (B) TYPE:amino acid
  - (D) TOPOLOGY:linear

30

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:H-CDR3-1
- (D) OTHER INFORMATION:hypervariable region

35

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 8:

Glu Glu Tyr Asp Tyr Asp Thr Leu Asp Tyr  
                                   5                                  10

(2) INFORMATION FOR SEQ ID NO: 9:

40

- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH:11 amino acids
  - (B) TYPE:amino acid
  - (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

- (A) NAME/KEY:H-CDR3-2
- (D) OTHER INFORMATION:hypervariable region

45

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:9:

Asp Arg Gly Gly Arg Asp Trp Tyr Phe Asp Val  
                                   5                                  10

50

(2) INFORMATION FOR SEQ ID NO: 10:

- (i) SEQUENCE CHARACTERISTICS:

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## (2) INFORMATION FOR SEQ ID NO: 14:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:11 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

## (ix) FEATURE:

- (A) NAME/KEY:L-CDR1-3
- (D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 14:

Lys Ala Ser Gln Asp Val Asn Thr Ala Val Ala  
5 10

## (2) INFORMATION FOR SEQ ID NO: 15:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:11 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

## (ix) FEATURE:

- (A) NAME/KEY:L-CDR1-4
- (D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:15:

Lys Ala Ser Gln Asp Val Thr Thr Asp Val Ala  
5 10

## (2) INFORMATION FOR SEQ ID NO: 16:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:7 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

## (ix) FEATURE:

- (A) NAME/KEY:L-CDR2-1
- (D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 16:

Leu Val Ser Asn Leu Glu Ser  
5

## (2) INFORMATION FOR SEQ ID NO: 17:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:7 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

## (ix) FEATURE:

- (A) NAME/KEY:L-CDR2-2
- (D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:17:

Leu Val Ser Asn Leu Asp Ser

5

(2) INFORMATION FOR SEQ ID NO: 18:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:7 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

(A) NAME/KEY:L-CDR2-3

(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 18:

Ser Ala Ser Tyr Arg Tyr Thr

5

(2) INFORMATION FOR SEQ ID NO: 19:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:8 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

(A) NAME/KEY:L-CDR3-1

(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:19:

Gln His Ile Arg Val Ala Tyr Thr

5

(2) INFORMATION FOR SEQ ID NO: 20:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:8 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

(A) NAME/KEY:L-CDR3-2

(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 20:

Gln His Ile Arg Gly Ala Tyr Thr

5

(2) INFORMATION FOR SEQ ID NO: 21:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:8 amino acids
- (B) TYPE:amino acid
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:protein

(ix) FEATURE:

(A) NAME/KEY:L-CDR3-3

(D) OTHER INFORMATION:hypervariable region

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:21:

5 Gln His Ile Glu Gly Ala Tyr Thr  
5

(2) INFORMATION FOR SEQ ID NO: 22:

10 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH:9 amino acids  
(B) TYPE:amino acid  
(D) TOPOLOGY:linear  
(ii) MOLECULE TYPE:protein  
(ix) FEATURE:  
15 (A) NAME/KEY:L-CDR3-4  
(D) OTHER INFORMATION:hypervariable region  
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 22:

Gln Gln His Tyr Ser Pro Pro Leu Thr  
5

20 (2) INFORMATION FOR SEQ ID NO: 23:

(i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH:9 amino acids  
(B) TYPE:amino acid  
(D) TOPOLOGY:linear  
25 (ii) MOLECULE TYPE:protein  
(ix) FEATURE:  
(A) NAME/KEY:L-CDR3-5  
(D) OTHER INFORMATION:hypervariable region  
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:23:

30 Gln Gln His Tyr Ser Thr Ala Trp Thr  
5

(2) INFORMATION FOR SEQ ID NO: 24:

35 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH:34 base pairs  
(B) TYPE:nucleic acid  
(C) STRANDEDNESS:single  
(D) TOPOLOGY:linear  
40 (ii) MOLECULE TYPE:cdna  
(iv) ANTISENSE:no  
(iii) HYPOTHETICAL:no  
(ix) FEATURE:  
(A) NAME/KEY:H Leader Sequence A  
(D) OTHER INFORMATION:R is A or G;  
45 S is C or G;  
K is G or T;  
Y is C or T;  
M is A or C.  
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 24:

50 GGGAATTCAT GRASTTSKGG YYTMARCTKG RTTT

34

(2) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:

55

- 5 (A) LENGTH:34 base pairs  
 (B) TYPE:nucleic acid  
 (C) STRANDEDNESS:single  
 (D) TOPOLOGY:linear  
 (ii) MOLECULE TYPE:cDNA  
 (iii) HYPOTHETICAL:no  
 (iv) ANTISENSE:no  
 (ix) FEATURE:  
 10 (A) NAME/KEY:H Leader Sequence R  
 (D) OTHER INFORMATION:S is C or G;  
 Y is C or T;  
 W is A or T;  
 R is A or G.  
 15 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:25:

GGGAATTCAT GRAATGSASC TGGGTYWTYC TCTT

34

(2) INFORMATION FOR SEQ ID NO: 26:

- 20 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH:18 base pairs  
 (B) TYPE:nucleic acid  
 (C) STRANDEDNESS:single  
 (D) TOPOLOGY:linear  
 (ii) MOLECULE TYPE:cDNA  
 25 (iii) HYPOTHETICAL:no  
 (iv) ANTISENSE:no  
 (ix) FEATURE:  
 (A) NAME/KEY:H Leader Sequence C  
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 26:

30 TTAAATGGTA TCCAGTGT

18

(2) INFORMATION FOR SEQ ID NO: 27:

- 35 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH:35 base pairs  
 (B) TYPE:nucleic acid  
 (C) STRANDEDNESS:single  
 (D) TOPOLOGY:linear  
 (ii) MOLECULE TYPE:cDNA  
 (iii) HYPOTHETICAL:no  
 40 (iv) ANTISENSE:no  
 (ix) FEATURE:  
 (A) NAME/KEY:H Constant Region  
 (D) OTHER INFORMATION:R is A or G;  
 K is G or T;  
 N is inosine.  
 45 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:27:

CCCAAGCTTC CAGGGRCCAR KGGATARACN GRTGG

35

(2) INFORMATION FOR SEQ ID NO: 28:

- 50 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH:32 base pairs  
 (B) TYPE:nucleic acid  
 (C) STRANDEDNESS:single  
 (D) TOPOLOGY:linear

55

5 (ii) MOLECULE TYPE:cDNA  
 (iii) HYPOTHETICAL:no  
 (iv) ANTISENSE:no  
 (ix) FEATURE:  
     (A) NAME/KEY:L Leader Sequence A  
     (D) OTHER INFORMATION:R is A or G;  
                                     K is G or T;  
                                     W is A or T;  
                                     Y is C or T.  
 10 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 28:  
 GCGAATTCAT GRAGWCACAK WCYCAGGTCT TT 32

15 (2) INFORMATION FOR SEQ ID NO: 29:  
 (i) SEQUENCE CHARACTERISTICS:  
     (A) LENGTH:33 base pairs  
     (B) TYPE:nucleic acid  
     (C) STRANDEDNESS:single  
     (D) TOPOLOGY:linear  
 20 (ii) MOLECULE TYPE:cDNA  
 (iii) HYPOTHETICAL:no  
 (iv) ANTISENSE:no  
 (ix) FEATURE:  
     (A) NAME/KEY:L Leader Sequence B  
 25 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 29:  
 GGAATTCAAT GGAGACAGAC ACACTCCTGC TAT 33

30 (2) INFORMATION FOR SEQ ID NO: 30:  
 (i) SEQUENCE CHARACTERISTICS:  
     (A) LENGTH:30 base pairs  
     (B) TYPE:nucleic acid  
     (C) STRANDEDNESS:single  
     (D) TOPOLOGY:linear  
 35 (ii) MOLECULE TYPE:cDNA  
 (iii) HYPOTHETICAL:no  
 (iv) ANTISENSE:no  
 (ix) FEATURE:  
     (A) NAME/KEY:L constant  
 40 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 30:  
 CCCAAGCTTA CTGGATGGTG GGAAGATGGA 30

45 (2) INFORMATION FOR SEQ ID NO: 31:  
 (i) SEQUENCE CHARACTERISTICS:  
     (A) LENGTH:357 base pairs  
     (B) TYPE:nucleic acid  
     (C) STRANDEDNESS:double  
     (D) TOPOLOGY:linear  
 50 (ii) MOLECULE TYPE:mRNA  
 (iii) HYPOTHETICAL:no  
 (iv) ANTISENSE:no  
 (vi) ORIGINAL SOURCE:  
     (A) ORGANISM:mouse  
 55 (ix) FEATURE:

(A) NAME/KEY:Idio 3 H chain variable/Idio 17 H chain variable  
(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 31:

GAG GTT CAG CTC GAG CAG TCT GGG ACT GTG CTG GCA AGG CCT GGG GCT 48  
Glu Val Gln Leu Gln Gln Ser Gly Thr Val Leu Ala Arg Pro Gly Ala  
5 10 15

TCA GTG AAG ATG TCC TGC AAG GCT TCG GGC TAC ACC TTT AAC AGC TAC 96  
Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Asn Ser Tyr  
20 25 30

TGG ATG CAC TGG GTA AAA CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT 144  
Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile  
35 40 45

GGC GCG ATT TAT CCT GGA AAT AGT GAT ATT AGC TAC AGC CAG AAC TTT 192  
Gly Ala Ile Tyr Pro Gly Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe  
50 55 60

AAG GAC AGG GCC AAA CTG ACT GCC GTC ACA TCC ACC AGC ACT GCC TAC 240  
Lys Asp Arg Ala Lys Leu Thr Ala Val Thr Ser Thr Ser Thr Ala Tyr  
65 70 75 80

ATG GAA CTC AGA AGC CTG ACA AAT GAG GAC TCT GCG GTC TAT TTC TGT 288  
Met Glu Leu Arg Ser Leu Thr Asn Glu Asp Ser Ala Val Tyr Phe Cys  
85 90 95

ACA AAA GAG GAA TAT GAT TAC GAC ACC CTG GAC TAC TGG GGT CAA GGA 336  
Thr Lys Glu Glu Tyr Asp Tyr Asp Thr Leu Asp Tyr Trp Gly Gln Gly  
100 105 110

ACC TCA GTC ACC GTC TCC TCA 357  
Thr Ser Val Thr Val Ser Ser  
115

(2) INFORMATION FOR SEQ ID NO: 32:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH:366 base pairs

(B) TYPE:nucleic acid

(C) STRANDEDNESS:double

(D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

(A) ORGANISM:mouse

(ix) FEATURE:

(A) NAME/KEY:Idio 20 H chain variable

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 32:

GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG CCT GGG GGT 48  
Glu Val Lys Leu Val Glu Ser Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

TCT CTC AGA CTC TCC TGT GCA ACT TCT GGG TTA ACC TTC ACT GAT TAC 96  
Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Leu Thr Phe Thr Asp Tyr  
20 25 30



TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GAA CTT GAA TGG TTG 144  
Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Glu Leu Glu Trp Leu  
35 40 45

GGT TTT ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA GAC TAC AGT GCA 192  
Gly Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr Asp Tyr Ser Ala  
50 55 60

TCT GTG AAG GGT CGG TTC ACC ATC TCC AGA CAT AAT CCC CAA AGC ATC 240  
Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Pro Gln Ser Ile  
65 70 75 80

CTC TAT CTT CAA ATG AAC ACC CTG ACA ACT GAG GAC AGT GCC ACT TAT 288  
Leu Tyr Leu Gln Met Asn Thr Leu Thr Thr Glu Asp Ser Ala Thr Tyr  
85 90 95

TAC TGT GCA AGA GAT AGG GGG GGG AGG GAC TGG TAC TTC GAT GTC TGG 336  
Tyr Cys Ala Arg Asp Arg Gly Gly Arg Asp Trp Tyr Phe Asp Val Trp  
100 105 110

GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA 366  
Gly Ala Gly Thr Thr Val Thr Val Ser Ser  
115 120

(2) INFORMATION FOR SEQ ID NO: 33:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:366 base pairs
- (B) TYPE:nucleic acid
- (C) STRANDEDNESS:double
- (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

(A) ORGANISM:mouse

(ix) FEATURE:

(A) NAME/KEY:Idio 27 H chain variable

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 33:

GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG CCT GGG GGT 48  
Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly  
5 10 15

TCT CTG AGA CTC TCC TGT GCA ACT TCT GGG TTC ACC TTC ACT GAT TAC 96  
Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Phe Thr Phe Thr Asp Tyr  
20 25 30

TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG 144  
Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu  
35 40 45

GGT TTT ATT AGA AAC AAA GCT AAT TAT TAC ACA ACA GAG TAC AGT GCA 192  
Gly Phe Ile Arg Asn Lys Ala Asn Tyr Tyr Thr Thr Glu Tyr Ser Ala  
50 55 60

TCT GTG AAG GGT CGG TTC ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC 240  
 Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Gln Ser Ile  
 65 70 75 80

CTC TAT CTT CAA ATG AAC ACC CTG AGA GCT GAG GAC AGT GCC ACT TAT 288  
 Leu Gln Met Asn Thr Leu Thr Leu Arg Ala Glu Asp Ser Ala Thr Tyr  
 85 90 95

TAC TGT GCA AGA GAT GGG TTC CTA CGG GAC TGG TAC TTC GAT GTC TGG 336  
 Tyr Cys Ala Arg Asp Gly Phe Leu Arg Asp Trp Tyr Phe Asp Val Trp  
 100 105 110

GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA 366  
 Gly Ala Gly Thr Thr Val Thr Val Ser Ser  
 115 120

(2) INFORMATION FOR SEQ ID NO: 34:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:363 base pairs  
 (B) TYPE:nucleic acid  
 (C) STRANDEDNESS:double  
 (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

(A) ORGANISM:mouse

(ix) FEATURE:

(A) NAME/KEY:Idio 33 H chain variable

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 34:

GAG GTT CAG CTC CAG CAG TCT GGG GCT GAA CTG GCA AGA CCT GGG GCT 48  
 Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Ala Arg Pro Gly Ala  
 5 10 15

TCA GTG AAC TTG TCC TGC AAG GCT TCT GGC TAC ACC TTT ACT AAC TAC 96  
 Ser Val Asn Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Asn Tyr  
 20 25 30

TGG ATG CAG TGG GTA AAA CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT 144  
 Trp Met Gln Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile  
 35 40 45

GGG GCT ATT TAT CCT GGA GAT GGT GAT ACT AGG TAC ACT CAG AAG TTC 192  
 Gly Ala Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr Thr Gln Lys Phe  
 50 55 60

AAG GGC AAG GCC ACA TTG ACT GCA GCT AAA TCC TCC AGC ACA GCC TAC 240  
 Lys Gly Lys Ala Thr Leu Thr Ala Ala Lys Ser Ser Ser Thr Ala Tyr  
 65 70 75 80

ATG CAA CTC AGC AGC TTG GCA TCT GAG GAC TCT GCG GTC TAT TAC TGT 288  
 Met Gln Leu Ser Ser Leu Ala Ser Glu Asp Ser Ala Val Tyr Tyr Cys  
 85 90 95

GCA AGA TCG GGC TAC TAT GGT AGC TTC GTT GGG TTT GCT TAC TGG GGC 336  
 Ala Arg Ser Gly Tyr Tyr Gly Ser Phe Val Gly Phe Ala Tyr Trp Gly  
                   100                  105                  110

CAA GGG ACT CTG GTC ACT GTC TCT GCA 363  
 Gln Gly Thr Leu Val Thr Val Ser Ala  
                   115                  120

(2) INFORMATION FOR SEQ ID NO: 35:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:336 base pairs  
 (B) TYPE:nucleic acid  
 (C) STRANDEDNESS:double  
 (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

(A) ORGANISM:mouse

(ix) FEATURE:

(A) NAME/KEY:Idio 3 L chain variable

(xi) SEQUENCE DESCRIPTION:SEQ ID NO: 35:

GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CCT CTG 48  
 Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Pro Leu  
                   5                  10                  15

GGG CAG AGG GCC ACC ATC TCA TAC AGG GCC AGC AAA AGT GTG CAG TTA 96  
 Gly Gln Arg Ala Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Gln Leu  
                   20                  25                  30

CAT CTG GCT ATA GTT TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG 144  
 His Leu Ala Ile Val Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln  
                   35                  40                  45

CCA CCC AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC 192  
 Pro Pro Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val  
                   50                  55                  60

CCT GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC 240  
 Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn  
                   65                  70                  75                  80

ATC CAT CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC 288  
 Ile His Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His  
                   85                  90                  95

ATT AGG GTA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA 336  
 Ile Arg Val Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
                   100                  105                  110

(2) INFORMATION FOR SEQ ID NO: 36:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:330 base pairs

(B) TYPE:nucleic acid  
 (C) STRANDEDNESS:double  
 (D) TOPOLOGY:linear  
 5 (ii) MOLECULE TYPE:mRNA  
 (iii) HYPOTHETICAL:no  
 (iv) ANTISENSE:no  
 (vi) ORIGINAL SOURCE:  
 (A) ORGANISM:mouse  
 10 (ix) FEATURE:  
 (A) NAME/KEY:Idio 17 L chain variable  
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 36:

GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG	48
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly	
5 10 15	
CAG AGG GCC TCC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT	96
Gln Arg Ala Ser Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser	
20 25 30	
GGC TAT AGT TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG CCA CCC	144
Gly Tyr Ser Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln Pro Pro	
35 40 45	
AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC CCT GCC	192
Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val Pro Ala	
50 55 60	
AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT	240
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His	
65 70 75 80	
CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT AGG	288
Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Arg	
85 90 95	
GGA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA	330
Gly Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys	
100 105 110	

## (2) INFORMATION FOR SEQ ID NO: 37:

40 (1) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH:330 base pairs  
 (B) TYPE:nucleic acid  
 (C) STRANDEDNESS:double  
 (D) TOPOLOGY:linear  
 45 (ii) MOLECULE TYPE:mRNA  
 (iii) HYPOTHETICAL:no  
 (iv) ANTISENSE:no  
 (vi) ORIGINAL SOURCE:  
 (A) ORGANISM:mouse  
 50 (ix) FEATURE:  
 (A) NAME/KEY:Idio 20 L chain variable  
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 37:

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GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG	48
Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly	
5 10 15	
CAG AGG GCC ACC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT	96
Gln Arg Ala Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser	
20 25 30	
GGC TAT AGT TAT ATG CAC TGG AAC CAA CAG AGA CCA GGA CAG CCA CCC	144
Gly Tyr Ser Tyr Met His Trp Asn Gln Gln Arg Pro Gly Gln Pro Pro	
35 40 45	
AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAC TCT GGG GTC CCT GCC	192
Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Asp Ser Gly Val Pro Ala	
50 55 60	
AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT	240
Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His	
65 70 75 80	
CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT GAG	288
Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Cys Gln His Ile Glu	
85 90 95	
GGA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA	330
Gly Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys	
100 105 110	

## (2) INFORMATION FOR SEQ ID NO: 38:

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- (i) SEQUENCE CHARACTERISTICS:
  - (A) LENGTH:321 base pairs
  - (B) TYPE:nucleic acid
  - (C) STRANDEDNESS:double
  - (D) TOPOLOGY:linear
- (ii) MOLECULE TYPE:mRNA
- (iii) HYPOTHETICAL:no
- (iv) ANTISENSE:no
- (vi) ORIGINAL SOURCE:
  - (A) ORGANISM:mouse
- (ix) FEATURE:
  - (A) NAME/KEY:Idio 27 L chain variable
- (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 38:

45  
50  
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GAC ATT GTG ATG ACC CAG TCT CAC AAA TTC ATG TCC ACA TCA GTA GGA	48
Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly	
5 10 15	
GAC AGG GTC AGT ATC ACC TGC AAG GCC AGT CAG GAT GTG AAT ACT GCT	96
Asp Arg Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala	
20 25 30	
GTA GCC TGG TAT CAA CAG AAA CCA GGA CAA TCT CCT AAA CTA CTG CTT	144
Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Leu	
35 40 45	

5 TAC TCG GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT CAC TTC ACT GGC 192  
 Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp His Phe Thr Gly  
 50 55 60  
 AGT GGA TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC GGT GTG CAG GCT 240  
 Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Gly Val Gln Ala  
 65 70 75 80  
 10 GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT AGT CCT CCT CTC 288  
 Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Pro Pro Leu  
 85 90 95  
 15 ACG TTC GGT GCT GGG ACC AAG CTG GAA CTG AAA 321  
 Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys  
 100 105

(2) INFORMATION FOR SEQ ID NO: 39:

- 20 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH:321 base pairs  
 (B) TYPE:nucleic acid  
 (C) STRANDEDNESS:double  
 (D) TOPOLOGY:linear  
 25 (ii) MOLECULE TYPE:mRNA  
 (iii) HYPOTHETICAL:no  
 (iv) ANTISENSE:no  
 (vi) ORIGINAL SOURCE:  
 (A) ORGANISM:mouse  
 (ix) FEATURE:  
 (A) NAME/KEY:Idio 33 L chain variable  
 30 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 39:

GAC ATT GTG ATG ACA CAG TCT CAC AAA TTC ATG TCC ACA TCA GTT GGA 48  
 Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly  
 5 10 15  
 35 GAC AGG GTC ACC ATC ACC TGC AAG GCC AGT CAG GAT GTG ACT ACT GAT 96  
 Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Val Thr Thr Asp  
 20 25 30  
 40 GTA GCC TGG TAT CAA CAG AAA CCA CGA CAA TCT CCT AAA CTA CTG ATT 144  
 Val Ala Trp Tyr Gln Gln Lys Pro Arg Gln Ser Pro Lys Leu Leu Ile  
 35 40 45  
 TAC TCG GCA TCC TAT CGG TAC ACT GGA GTC CCT GAT CGC TTC ACT GGC 192  
 Tyr Ser Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp Arg Phe Thr Gly  
 50 55 60  
 45 AGT GGA TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC AGT GTG CAG GCT 240  
 Ser Gly Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Ser Val Gln Ala  
 65 70 75 80  
 50 GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT AGT ACT GCG TGG 288  
 Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Thr Ala Trp  
 85 90 95

ACG TTC GGT GGT GGC ACC AAG CTG GAA ATC AAA  
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
 100 105

321

## (2) INFORMATION FOR SEQ ID NO: 40:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:399 base pairs  
 (B) TYPE:nucleic acid  
 (C) STRANDEDNESS:double  
 (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

(A) ORGANISM:mouse

(ix) FEATURE:

(A) NAME/KEY:Clone 3GB1

(xi) SEQUENCE DESCRIPTION:SEQ ID NO:40:

CTG TCG GTA ACT TCA GGG GTC TAC TCA GAG GTT CAG CTC GAG CAG TCT -48  
 Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln Gln Ser  
 -5 1 5

GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC AAG 96  
 Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys Lys  
 10 15 20

GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA CAG 144  
 Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys Gln  
 25 30 35

AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA AAT 192  
 Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly Asn  
 40 45 50 55

AGT GAT ATT AGC TAC AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG ACT 240  
 Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu Thr  
 60 65 70

GCC GTC ACA TCC ACC AGC ACT GCC TAC ATG GAA CTC AGA AGC CTG ACA 288  
 Ala Val Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu Thr  
 75 80 85

AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT TAC 336  
 Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asp Tyr  
 90 95 100

GAC ACC CTG GAC TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TCC TCA 384  
 Asp Thr Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser Ser  
 105 110 115

GCC AAA ACG ACA CCC 399  
 Ala Lys Thr Thr Pro  
 120

## (2) INFORMATION FOR SEQ ID NO: 41:

- (1) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH:402 base pairs  
 (B) TYPE:nucleic acid  
 (C) STRANDEDNESS:double  
 (D) TOPOLOGY:linear  
 (ii) MOLECULE TYPE:mRNA  
 (iii) HYPOTHETICAL:no  
 (iv) ANTISENSE:no  
 (vi) ORIGINAL SOURCE:  
 (A) ORGANISM:mouse  
 (ix) FEATURE:  
 (A) NAME/KEY:Clone 17GB7  
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 41:

```

ATT GTG TCG GTA ACT TCA GGG GTC TAC TCA GAG GTT CAG CTC GAG CAG 48
Ile Leu Ser Val Thr Ser Gly Val Tyr Ser Glu Val Gln Leu Gln Gln
-10                               -5                               1                               5
TCT GGG ACT GTG CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG TCC TGC 96
Ser Gly Thr Val Leu Ala Arg Pro Gly Ala Ser Val Lys Met Ser Cys
10                               15                               20
AAG GCT TCG GGC TAC ACC TTT AAC AGC TAC TGG ATG CAC TGG GTA AAA 144
Lys Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Trp Met His Trp Val Lys
25                               30                               35
CAG AGG CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG ATT TAT CCT GGA 192
Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala Ile Tyr Pro Gly
30                               40                               45                               50
AAT AGT GAT ATT AGC TAC AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG 240
Asn Ser Asp Ile Ser Tyr Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu
55                               60                               65                               70
ACT GCC GTC ACA TCC ACC AGC ACT GCC TAC ATG GAA CTC AGA AGC CTG 288
Thr Ala Val Thr Ser Thr Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu
35                               75                               80                               85
ACA AAT GAG GAC TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA TAT GAT 336
Thr Asn Glu Asp Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu Tyr Asp
40                               90                               95                               100
TAC GAC ACC CTG GAC TAC TGG GGT CAA GGA ACC TCA GTC ACC GTC TCC 384
Tyr Asp Thr Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
105                               110                               115
TCA GCC AAA ACG ACA CCC
Ser Ala Lys Thr Thr Pro
120
402

```

## (2) INFORMATION FOR SEQ ID NO: 42:

- (1) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH:438 base pairs  
 (B) TYPE:nucleic acid



(C) STRANDEDNESS:double  
(D) TOPOLOGY:linear

5 (ii) MOLECULE TYPE:mRNA  
(iii) HYPOTHETICAL:no  
(iv) ANTISENSE:no  
(vi) ORIGINAL SOURCE:  
(A) ORGANISM:mouse  
(ix) FEATURE:  
10 (A) NAME/KEY:Clone 20GA2  
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:42:

ATG GAG TTC GGG CTA AAC TGG GTT TTC CTT GTA ACA CTT TTA AAT GGT 48  
Met Glu Phe Gly Leu Asn Trp Val Phe Leu Val Thr Leu Leu Asn Gly  
-15 -10 -5

15 ATC CAG TGT GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC TTG GTA CAG 96  
Ile Gln Cys Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Gln  
1 5 10

20 CCT GGG GGT TCT CTC AGA CTC TCC TGT GCA ACT TCT GGG TTA ACC TTC 144  
Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Leu Thr Phe  
15 20 25

25 ACT GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT CCA GGA AAG GAA CTT 192  
Thr Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro Pro Gly Lys Glu Leu  
30 35 40 45

GAA TGG TTG GGT TTT ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA GAC 240  
Glu Trp Leu Gly Phe Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr Asp  
50 55 60

30 TAC AGT GCA TCT GTG AAG GGT CGG TTC ACC ATC TCC AGA CAT AAT CCC 288  
Tyr Ser Ala Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Pro  
65 70 75

35 CAA AGC ATC CTC TAT CTT CAA ATG AAC ACC CTG ACA ACT GAG GAC AGT 336  
Gln Ser Ile Leu Tyr Leu Gln Met Asn Thr Leu Thr Thr Glu Asp Ser  
80 85 90

GCC ACT TAT TAC TGT GCA AGA GAT AGG GGG GGG AGG GAC TGG TAC TTC 384  
Ala Thr Tyr Tyr Cys Ala Arg Asp Arg Gly Gly Arg Asp Trp Tyr Phe  
95 100 105

40 GAT GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC TCC TCA GCC AAA ACG 432  
Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser Ala Lys Thr  
110 115 120 125

45 ACA CCC 438  
Thr Pro

## (2) INFORMATION FOR SEQ ID NO: 43:

50 (i) SEQUENCE CHARACTERISTICS:  
(A) LENGTH:411 base pairs  
(B) TYPE:nucleic acid  
(C) STRANDEDNESS:double  
(D) TOPOLOGY:linear

55

(ii) MOLECULE TYPE:mrna  
 (iii) HYPOTHETICAL:no  
 (iv) ANTISENSE:no  
 (vi) ORIGINAL SOURCE:  
       (A) ORGANISM:mouse  
 (ix) FEATURE:  
       (A) NAME/KEY:Clone 27GA5  
 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 43:

CTT GTA ACA CGT TTA AAT GGT ATC CAG TGT GAG GTG AAG CTG GTG GAG 48  
 Leu Val Thr Arg Leu Asn Gly Ile Gln Cys Glu Val Lys Leu Val Glu  
 -10 -5 1 5

TCT GGA GGA GGC TTG GTA CAG CCT GGG GGT TCT CTG AGA CTC TCC TGT 96  
 Ser Gly Gly Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys  
 10 15 20

GCA ACT TCT GGG TTC ACC TTC ACT GAT TAC TAC ATG AAC TGG GTC CGC 144  
 Ala Thr Ser Gly Phe Thr Phe Thr Asp Tyr Tyr Met Asn Trp Val Arg  
 20 25 30 35

CAG CCT CCA GGA AAG GCA CTT GAG TGG TTG GGT TTT ATT AGA AAC AAA 192  
 Gln Pro Pro Gly Lys Ala Leu Glu Trp Leu Gly Phe Ile Arg Asn Lys  
 40 45 50

GCT AAT TAT TAC ACA ACA GAG TAC AGT GCA TCT GTG AAG GGT CGG TTC 240  
 Ala Asn Tyr Tyr Thr Thr Glu Tyr Ser Ala Ser Val Lys Gly Arg Phe  
 55 60 65 70

ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC CTC TAT CTT CAA ATG AAC 288  
 Thr Ile Ser Arg Asp Asn Ser Gln Ser Ile Leu Gln Met Asn Thr Leu  
 75 80 85

ACC CTG AGA GCT GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA GAT GGG 336  
 Thr Leu Arg Ala Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg Asp Gly  
 90 95 100

TTC CTA CGG GAC TGG TAC TTC GAT GTC TGG GGC GCA GGG ACC ACG GTC 384  
 Phe Leu Arg Asp Trp Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val  
 105 110 115

ACC GTC TCC TCA GCC AAA ACG ACA CCC 411  
 Thr Val Ser Ser Ala Lys Thr Thr Pro  
 120 125

(2) INFORMATION FOR SEQ ID NO: 44:

(i) SEQUENCE CHARACTERISTICS:  
       (A) LENGTH:354 base pairs  
       (B) TYPE:nucleic acid  
       (C) STRANDEDNESS:double  
       (D) TOPOLOGY:linear  
 (ii) MOLECULE TYPE:mrna  
 (iii) HYPOTHETICAL:no  
 (iv) ANTISENSE:no  
 (vi) ORIGINAL SOURCE:  
       (A) ORGANISM:mouse

## (ix) FEATURE:

(A) NAME/KEY:Clone 3KB11

## (xi) SEQUENCE DESCRIPTION:SEQ ID NO:44:

GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CCT CTG 48  
 Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Pro Leu  
 5 10 15  
 GGG CAG AGG GCC ACC ATC TCA TAC AGG GCC AGC AAA AGT GTG CAG TTA 96  
 Gly Gln Arg Ala Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Gln Leu  
 20 25 30  
 CAT CTG GCT ATA GTT TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG 144  
 His Leu Ala Ile Val Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln  
 35 40 45  
 CCA CCC AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC 192  
 Pro Pro Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val  
 50 55 60  
 CCT GCC AGG TTC AGT GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC 240  
 Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn  
 65 70 75 80  
 ATC CAT CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC 288  
 Ile His Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His  
 85 90 95  
 ATT AGG GTA GCT TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA 336  
 Ile Arg Val Ala Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
 100 105 110  
 CGG GCT GAT GCT GCA CCA 354  
 Arg Ala Asp Ala Ala Pro  
 115

## (2) INFORMATION FOR SEQ ID NO: 45:

## (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH:438 base pairs  
 (B) TYPE:nucleic acid  
 (C) STANDEDNESS:double  
 (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

(iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

(A) ORGANISM:mouse

## (ix) FEATURE:

(A) NAME/KEY:Clone 17KB1

## (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 45:

CTA TGG GTA CTG CTG CTC TGG GTT CCA GGT TCC ACT GGT GAC ATT GTG 48  
 Leu Trp Val Leu Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Ile Val  
 -10 -5 1

5 CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG CAG AGG GCC 96  
 Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala  
 5 10 15  
 10 TCC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAT AGT 144  
 Ser Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser  
 20 25 30 35  
 15 TAT ATG CAC TGG AAC CAA CAG AAA CCA GGA CAG CCA CCC AGA CTC CTC 192  
 Tyr Met His Trp Asn Gln Gln Lys Pro Gly Gln Pro Pro Arg Leu Leu  
 40 45 50  
 20 ATC TAT CTT GTA TCC AAC CTA GAA TCT GGG GTC CCT GCC AGG TTC AGT 240  
 Ile Tyr Leu Val Ser Asn Leu Glu Ser Gly Val Pro Ala Arg Phe Ser  
 55 60 65  
 25 GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG 288  
 Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu  
 70 75 80  
 30 GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT AGG GGA GCT TAC 336  
 Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Arg Gly Ala Tyr  
 85 90 95  
 35 ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA CGG GCT GAT GCT GCA 384  
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala Asp Ala Ala  
 100 105 110 115  
 40 CCA ACT GTA TCC ATC TTC CCA CCA TCC AGT AAG CTT GGG AAA CGG TTC 432  
 Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Lys Leu Gly Lys Arg Phe  
 120 125 130  
 45 GCA CCG  
 Ala Pro 438

(2) INFORMATION FOR SEQ ID NO: 46:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 417 base pairs  
 (B) TYPE: nucleic acid  
 (C) STRANDEDNESS: double  
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: mRNA

(iii) HYPOTHETICAL: no

(iv) ANTISENSE: no

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: mouse

(ix) FEATURE:

- (A) NAME/KEY: Clone 20KB1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 46:

GGCCGCG GTGAGAACCG TTGGGAATTC ATG GAG ACA GAC ACA CTC CTG 48  
 Met Glu Thr Asp Thr Leu Leu  
 -20 -15

5 CTA TGG GTA CTG CTG CTC TGG GTT CCA GGT TCC ACT GGT GAC ATT GTG 96  
 Leu Trp Val Leu Leu Trp Val Pro Gly Ser Thr Gly Asp Ile Val  
 -10 -5 1

10 CTG ACA CAG TCT CCT GCT TCC TTA GCT GTA TCT CTG GGG CAG AGG GCC 144  
 Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly Gln Arg Ala  
 5 10 15

15 ACC ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT ACA TCT GGC TAT AGT 192  
 Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser Thr Ser Gly Tyr Ser  
 20 25 30

20 TAT ATG CAC TGG AAC CAA CAG AGA CCA GGA CAG CCA CCC AGA CTC CTC 240  
 Tyr Met His Trp Asn Gln Gln Arg Pro Gly Gln Pro Pro Arg Leu Leu  
 35 40 45

25 ATC TAT CTT GTA TCC AAC CTA GAC TCT GGG GTC CCT GCC AGG TTC AGT 288  
 Ile Tyr Leu Val Ser Asn Leu Asp Ser Gly Val Pro Ala Arg Phe Ser  
 50 55 60 65

30 GGC AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT CCT GTG GAG 336  
 Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn Ile His Pro Val Glu  
 70 75 80

35 GAG GAG GAT GCT GCA ACC TAT TAC TGT CAG CAC ATT GAG GGA GCT TAC 384  
 Glu Glu Asp Ala Ala Thr Tyr Tyr Cys Gln His Ile Glu Gly Ala Tyr  
 85 90 95

40 ACG TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA 417  
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
 100 105

## (2) INFORMATION FOR SEQ ID NO: 47:

35 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH:420 base pairs  
 (B) TYPE:nucleic acid  
 (C) STRANDEDNESS:single  
 (D) TOPOLOGY:linear

(ii) MOLECULE TYPE:mRNA

40 (iii) HYPOTHETICAL:no

(iv) ANTISENSE:no

(vi) ORIGINAL SOURCE:

(A) ORGANISM:mouse

(ix) FEATURE:

(A) NAME/KEY:Clone 27KA2

45 (xi) SEQUENCE DESCRIPTION:SEQ ID NO: 47:

GCGGCCGCGG TGAGAACCGT TTGGGAATTC ATC GAG ACA CAG TCC CAG 48  
 Met Glu Thr Gln Ser Gln  
 -20 -15

50 GTC TTT GTA TTC GTG TTT CTC TGG TTG TCT GGT GTT GAC GGA GAC ATT 96  
 Val Phe Val Phe Val Phe Leu Trp Leu Ser Gly Val Asp Gly Asp Ile  
 -10 -5 1

55

5 GTG ATG ACC CAG TCT CAC AAA TTC ATG TCC ACA TCA GTA GGA GAC AGG 144  
 Val Met Thr Gln Ser His Lys Phe Met Ser Thr Ser Val Gly Asp Arg  
 5 10 15  
 10 GTC AGT ATC ACC TGC AAG GCC AGT CAG GAT GTG AAT ACT GCT GTA GCC 192  
 Val Ser Ile Thr Cys Lys Ala Ser Gln Asp Val Asn Thr Ala Val Ala  
 20 25 30  
 10 TGG TAT CAA CAG AAA CCA GGA CAA TCT CCT AAA CTA CTG CTT TAC TCG 240  
 Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Leu Leu Leu Tyr Ser  
 35 40 45 50  
 15 GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT CAC TTC ACT GGC AGT GGA 288  
 Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp His Phe Thr Gly Ser Gly  
 55 60 65  
 20 TCT GGG ACG GAT TTC ACT TTC ACC ATC AGC GGT GTG CAG GCT GAA GAC 336  
 Ser Gly Thr Asp Phe Thr Phe Thr Ile Ser Gly Val Gln Ala Glu Asp  
 70 75 80  
 20 CTG GCA GTT TAT TAC TGT CAG CAA CAT TAT AGT CCT CCT CTC ACG TTC 384  
 Leu Ala Val Tyr Tyr Cys Gln Gln His Tyr Ser Pro Pro Leu Thr Phe  
 85 90 95  
 25 GGT GCT GGG ACC AAG CTG GAA CTG AAA CGG GCT GAT 420  
 Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala Asp  
 100 105 110

## (2) INFORMATION FOR SEQ ID NO: 48:

- 30 (i) SEQUENCE CHARACTERISTICS:  
 (A) LENGTH:360 base pairs  
 (B) TYPE:nucleic acid  
 (C) STRANDEDNESS:single  
 (D) TOPOLOGY:linear  
 35 (ii) MOLECULE TYPE:mRNA  
 (iii) HYPOTHETICAL:no  
 (iv) ANTISENSE:no  
 (vi) ORIGINAL SOURCE:  
 (A) ORGANISM:mouse  
 (ix) FEATURE:  
 (A) NAME/KEY:Clone 23KA26  
 40 (xi) SEQUENCE DESCRIPTION:SEQ ID NO:48

45 GGT GTT GAC GGA GAC ATT GTG ATG ACA CAG TCT CAC AAA TTC ATG TCC 48  
 Gly Val Asp Gly Asp Ile Val Met Thr Gln Ser His Lys Phe Met Ser  
 1 5 10  
 45 ACA TCA GTT GGA GAC AGG GTC ACC ATC ACC TGC AAG GCC AGT CAG GAT 96  
 Thr Ser Val Gly Asp Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp  
 15 20 25  
 50 GTG ACT ACT GAT GTA GCC TGG TAT CAA CAG AAA CCA CGA CAA TCT CCT 144  
 Val Thr Thr Asp Val Ala Trp Tyr Gln Gln Lys Pro Arg Gln Ser Pro  
 30 35 40

5	AAA	CTA	CTG	ATT	TAC	TCG	GCA	TCC	TAT	CGG	TAC	ACT	GGA	GTC	CCT	GAT	192
	Lys	Leu	Leu	Ile	Tyr	Ser	Ala	Ser	Tyr	Arg	Tyr	Thr	Gly	Val	Pro	Asp	
	45						50					55					
	CGC	TTC	ACT	GGC	AGT	GGA	TCT	GGG	ACG	GAT	TTC	ACT	TTC	ACC	ATC	AGC	240
	Arg	Phe	Thr	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Phe	Thr	Ile	Ser	
	60					65				70						75	
10	AGT	GTG	CAG	GCT	GAA	GAC	CTG	GCA	GTT	TAT	TAC	TGT	CAG	CAA	CAT	TAT	288
	Ser	Val	Gln	Ala	Glu	Asp	Leu	Ala	Val	Tyr	Tyr	Cys	Gln	Gln	His	Tyr	
					80					85					90		
15	AGT	ACT	GCG	TGG	ACG	TTC	GGT	GGT	GGC	ACC	AAG	CTG	GAA	ATC	AAA	CCG	336
	Ser	Thr	Ala	Trp	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys	Arg	
				95					100					105			
	GCT	GAT	GCT	GCA	CCA	ACT	GTA	TCC									360
	Ala	Asp	Ala	Ala	Pro	Thr	Val	Ser									
			110					115									

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## 25 Claims

1. An immunoglobulin H chain variable region fragment which contains a hypervariable region CDR1 having an amino acid sequence selected from

30

(1) Ser Tyr Trp Met His;  
Asp Tyr Tyr Met Asn; and  
Asn Tyr Trp Met Gln,

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a hypervariable region CDR2 having an amino acid sequence selected from

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(2) Ala Ile Tyr Pro Gly Asn Ser  
Asp Ile Ser Tyr Ser Gln Asn  
Phe Lys Asp;

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Phe Ile Arg Asn Lys Ala  
Asn Leu Tyr Thr Thr Asp  
Tyr Ser Ala Ser Val Lys  
Gly;

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Phe Ile Arg Asn Lys Ala  
Asn Tyr Tyr Thr Thr Glu  
Tyr Ser Ala Ser Val Lys  
Gly; and

55

Ala Ile Tyr Pro Gly Asp  
Gly Asp Thr Arg Tyr Thr  
Gln Lys Phe Lys Gly,

and a hypervariable region CDR<sub>H</sub> having an amino acid sequence selected from

(3) Glu Glu Tyr Asp Tyr Asp  
 Thr Leu Asp Tyr;  
 Asp Arg Gly Gly Arg Asp  
 Trp Tyr Phe Asp Val;  
 Asp Gly Phe Leu Arg Asp  
 Trp Tyr Phe Asp Val; and  
 Ser Gly Tyr Tyr Gly Ser  
 Phe Val Gly Phe Ala Tyr .

2. An immunoglobulin H chain variable region fragment having the following amino acid sequence

Glu Val Gln Leu Gln Gln Ser Gly Thr Val  
 Leu Ala Arg Pro Gly Ala Ser Val Lys Met  
 Ser Cys Lys Ala Ser Gly Tyr Thr Phe Asn  
 Ser Tyr Trp Met His Trp Val Lys Gln Arg  
 Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala  
 Ile Tyr Pro Gly Asn Ser Asp Ile Ser Tyr  
 Ser Gln Asn Phe Lys Asp Arg Ala Lys Leu  
 Thr Ala Val Thr Ser Thr Ser Thr Ala Tyr  
 Met Glu Leu Arg Ser Leu Thr Asn Glu Asp  
 Ser Ala Val Tyr Phe Cys Thr Lys Glu Glu  
 Tyr Asp Tyr Asp Thr Leu Asp Tyr Trp Gly  
 Gln Gly Thr Ser Val Thr Val Ser Ser .



3. An immunoglobulin H chain variable region fragment having the following amino acid sequence

5           Glu Val Lys Leu Val Glu Ser Gly Gly Gly  
           Leu Val Gln Pro Gly Gly Ser Leu Arg Leu  
           Ser Cys Ala Thr Ser Gly Phe Thr Phe Thr  
           Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro  
 10          Pro Gly Lys Ala Leu Glu Trp Leu Gly Phe  
           Ile Arg Asn Lys Ala Asn Tyr Tyr Thr Thr  
           Glu Tyr Ser Ala Ser Val Lys Gly Arg Phe  
           Thr Ile Ser Arg Asp Asn Ser Gln Ser Ile  
 15          Leu Tyr Leu Gln Met Asn Thr Leu Arg Ala  
           Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg  
           Asp Gly Phe Leu Arg Asp Trp Tyr Phe Asp  
 20          Val Trp Gly Ala Gly Thr Thr Val Thr Val  
           Ser Ser.

- 25 4. An immunoglobulin H chain variable region fragment having the following amino acid sequence

30           Glu Val Lys Leu Val Glu Ser Gly Gly Gly  
           Leu Val Gln Pro Gly Gly Ser Leu Arg Leu  
           Ser Cys Ala Thr Ser Gly Leu Thr Phe Thr  
           Asp Tyr Tyr Met Asn Trp Val Arg Gln Pro  
           Pro Gly Lys Glu Leu Glu Trp Leu Gly Phe  
 35          Ile Arg Asn Lys Ala Asn Leu Tyr Thr Thr  
           Asp Tyr Ser Ala Ser Val Lys Gly Arg Phe  
           Thr Ile Ser Arg Asp Asn Pro Gln Ser Ile  
           Leu Tyr Leu Gln Met Asn Thr Leu Thr Thr  
 40          Glu Asp Ser Ala Thr Tyr Tyr Cys Ala Arg  
           Asp Arg Gly Gly Arg Asp Trp Tyr Phe Asp  
           Val Trp Gly Ala Gly Thr Thr Val Thr Val  
 45          Ser Ser.

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5. An immunoglobulin H chain variable region fragment having the following amino acid sequence

5      Glu Val Gln Leu Gln Gln Ser Gly Ala Glu  
       Leu Ala Arg Pro Gly Ala Ser Val Asn Leu  
       Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr  
       Asn Tyr Trp Met Gln Trp Val Lys Gln Arg  
 10     Pro Gly Gln Gly Leu Glu Trp Ile Gly Ala  
       Ile Tyr Pro Gly Asp Gly Asp Thr Arg Tyr  
       Thr Gln Lys Phe Lys Gly Lys Ala Thr Leu  
       Thr Ala Ala Lys Ser Ser Ser Thr Ala Tyr  
 15     Met Gln Leu Ser Ser Leu Ala Ser Glu Asp  
       Ser Ala Val Tyr Tyr Cys Ala Arg Ser Gly  
       Tyr Tyr Gly Ser Phe Val Gly Phe Ala Tyr  
 20     Trp Gly Gln Gly Thr Leu Val Thr Val Ser  
       Ala .

- 25 6. DNA and RNA fragments each encoding an immunoglobulin H chain variable region fragment which contains a base sequence encoding a hypervariable region CDR1 having an amino acid sequence selected from

(1) Ser Tyr Trp Met His;  
 30      Asp Tyr Tyr Met Asn; and  
       Asn Tyr Trp Met Gln ,

35 a base sequence encoding a hypervariable region CDR2 having an amino acid sequence selected from

(2) Ala Ile Tyr Pro Gly Asn Ser  
       Asp Ile Ser Tyr Ser Gln Asn  
 40      Phe Lys Asp;  
       Phe Ile Arg Asn Lys Ala  
       Asn Leu Tyr Thr Thr Asp  
       Tyr Ser Ala Ser Val Lys  
 45      Gly;  
       Phe Ile Arg Asn Lys Ala  
       Asn Tyr Tyr Thr Thr Glu  
 50      Tyr Ser Ala Ser Val Lys  
       Gly; and  
       Ala Ile Tyr Pro Gly Asp  
       Gly Asp Thr Arg Tyr Thr  
 55      Glu Lys Phe Lys Gly ,

a base sequence encoding a hypervariable region CDR3 having an amino acid sequence selected from

(3) Glu Glu Tyr Asp Tyr Asp  
 Thr Leu Asp Tyr;  
 Asp Arg Gly Gly Arg Asp  
 Trp Tyr Phe Asp Val;  
 Asp Gly Phe Leu Arg Asp  
 Trp Tyr Phe Asp Val; and  
 Ser Gly Tyr Tyr Gly Ser  
 Phe Val Gly Phe Ala Tyr .

7. An immunoglobulin H chain variable region fragment having following base sequence

GAG GTT CAG CTC CAG CAG TCT GGG ACT GTG  
 CTG GCA AGG CCT GGG GCT TCA GTG AAG ATG  
 TCC TGC AAG GCT TCG GGC TAC ACC TTT AAC  
 AGC TAC TGG ATG CAC TGG GTA AAA CAG AGG  
 CCT GGA CAG GGT CTG GAA TGG ATT GGC GCG  
 ATT TAT CCT GGA AAT AGT GAT ATT AGC TAC  
 AGC CAG AAC TTT AAG GAC AGG GCC AAA CTG  
 ACT GCC GTC ACA TCC ACC AGC ACT GCC TAC  
 ATG GAA CTC AGA AGC CTG ACA AAT GAG GAC  
 TCT GCG GTC TAT TTC TGT ACA AAA GAG GAA  
 TAT GAT TAC GAC ACC CTG GAC TAC TGG GGT  
 CAA GGA ACC TCA GTC ACC GTC TCC TCA.

8. An immunoglobulin H chain variable region fragment having the following base sequence

5 GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC  
 TTG GTA CAG CCT GGG GGT TCT CTC AGA CTC  
 TCC TGT GCA ACT TCT GGG TTA ACC TTC ACT  
 GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT  
 10 CCA GGA AAG GAA CTT GAA TGG TTG GGT TTT  
 ATT AGA AAC AAA GCT AAT CTT TAC ACA ACA  
 GAC TAC AGT GCA TCT GTG AAG GGT CGG TTC  
 ACC ATC TCC AGA GAT AAT CCC CAA AGC ATC  
 15 CTC TAT CTT CAA ATG AAC ACC CTG ACA ACT  
 GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA  
 GAT AGG GGG GGG AGG GAC TGG TAC TTC GAT  
 20 GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC  
 TCC TCA .

- 25 9. An immunoglobulin H chain variable region fragment having the following base sequence

30 GAG GTG AAG CTG GTG GAG TCT GGA GGA GGC  
 TTG GTA CAG CCT GGG GGT TCT CTG AGA CTC  
 TCC TGT GCA ACT TCT GGG TTC ACC TTC ACT  
 GAT TAC TAC ATG AAC TGG GTC CGC CAG CCT  
 CCA GGA AAG GCA CTT GAG TGG TTG GGT TTT  
 35 ATT AGA AAC AAA GCT AAT TAT TAC ACA ACA  
 GAG TAC AGT GCA TCT GTG AAG GGT CGG TTC  
 ACC ATC TCC AGA GAT AAT TCC CAA AGC ATC  
 40 CTC TAT CTT CAA ATG AAC ACC CTG AGA GCT  
 GAG GAC AGT GCC ACT TAT TAC TGT GCA AGA  
 GAT GGG TTC CTA CGG GAC TGG TAC TTC GAT  
 45 GTC TGG GGC GCA GGG ACC ACG GTC ACC GTC  
 TCC TCA .

10. An immunoglobulin H chain variable region fragment having the following base sequence

5 GAG GTT CAG CTC CAG CAG TCT GGG GCT GAA  
 CTG GCA AGA CCT GGG GCT TCA GTG AAC TTG  
 TCC TGC AAG GCT TCT GGC TAC ACC TTT ACT  
 AAC TAC TGG ATG CAG TGG GTA AAA CAG AGG  
 10 CCT GGA CAG GGT CTG GAA TGG ATT GGG GCT  
 ATT TAT CCT GGA GAT GGT GAT ACT AGG TAC  
 ACT CAG AAG TTC AAG GGC AAG GCC ACA TTG  
 ACT GCA GCT AAA TCC TCC AGC ACA GCC TAC  
 15 ATG CAA CTC AGC AGC TTG GCA TCT GAG GAC  
 TCT GCG GTC TAT TAC TGT GCA AGA TCG GGC  
 TAC TAT GGT AGC TTC GTT GGG TTT GCT TAC  
 TGG GGC CAA GGG ACT CTG GTC ACT GTC TCT  
 20 GCA .

25 11. An immunoglobulin L chain variable region fragment which contains a hypervariable region CDR1 having an amino acid sequence selected from

(1) Tyr Arg Ala Ser Lys Ser Val  
 30 Gln Leu His Leu Ala Ile Val  
 Tyr Met His;  
 Tyr Arg Ala Ser Lys Ser Val  
 Ser Thr Ser Gly Tyr Ser Tyr  
 35 Met His;  
 Lys Ala Ser Gln Asp Val Asn  
 Thr Ala Val Ala; and  
 40 Lys Ala Ser Gln Asp Val Thr  
 Thr Asp Val Ala ,

45 a hypervariable region CDR2 having an amino acid sequence selected from

(2) Leu Val Ser Asn Leu Glu Ser;  
 Leu Val Ser Asn Leu Asp Ser; and  
 50 Ser Ala Ser Tyr Arg Tyr Thr ,

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and a hypervariable region CDR3 having an amino acid sequence selected from

- (3) Gln His Ile Arg Val Ala Tyr  
Thr;  
Gln His Ile Arg Gly Ala Tyr  
Thr;  
Gln His Ile Glu Gly Ala Tyr  
Thr;  
Gln Gln His Tyr Ser Pro Pro  
Leu Thr; and  
Gln Gln His Tyr Ser Thr Ala  
Trp Thr .

12. An immunoglobulin L chain variable region fragment having the following amino acid sequence

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser  
Leu Ala Val Ser Pro Leu Gly Gln Arg Ala  
Thr Ile Ser Tyr Arg Ala Ser Lys Ser Val  
Gln Leu His Leu Ala Ile Val Tyr Met His  
Trp Asn Gln Gln Lys Pro Gly Gln Pro Pro  
Arg Leu Leu Ile Tyr Leu Val Ser Asn Leu  
Glu Ser Gly Val Pro Ala Arg Phe Ser Gly  
Ser Gly Ser Gly Thr Asp Phe Thr Leu Asn  
Ile His Pro Val Glu Glu Glu Asp Ala Ala  
Thr Tyr Tyr Cys Gln His Ile Arg Val Ala  
Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu  
Ile Lys .

13. An immunoglobulin L chain variable region fragment having the following amino acid sequence

5           Asp Ile Val Leu Thr Gln Ser Pro Ala Ser  
           Leu Ala Val Ser Leu Gly Gln Arg Ala Ser  
           Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser  
           Thr Ser Gly Tyr Ser Tyr Met His Trp Asn  
 10          Gln Gln Lys Pro Gly Gln Pro Pro Arg Leu  
           Leu Ile Tyr Leu Val Ser Asn Leu Glu Ser  
           Gly Val Pro Ala Arg Phe Ser Gly Ser Gly  
           Ser Gly Thr Asp Phe Thr Leu Asn Ile His  
 15          Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr  
           Tyr Cys Gln His Ile Arg Gly Ala Tyr Thr  
           Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys.

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14. An immunoglobulin L chain variable region fragment having the following amino acid sequence

25           Asp Ile Val Leu Thr Gln Ser Pro Ala Ser  
           Leu Ala Val Ser Leu Gly Gln Arg Ala Thr  
           Ile Ser Tyr Arg Ala Ser Lys Ser Val Ser  
           Thr Ser Gly Tyr Ser Tyr Met His Trp Asn  
 30          Gln Gln Arg Pro Gly Gln Pro Pro Arg Leu  
           Leu Ile Tyr Leu Val Ser Asn Leu Asp Ser  
           Gly Val Pro Ala Arg Phe Ser Gly Ser Gly  
           Ser Gly Thr Asp Phe Thr Leu Asn Ile His  
 35          Pro Val Glu Glu Glu Asp Ala Ala Thr Tyr  
           Tyr Cys Gln His Ile Glu Gly Ala Tyr Thr  
           Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys.

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15. An immunoglobulin L chain variable region fragment having the following amino acid sequence

5 Asp Ile Val Met Thr Gln Ser His Lys Phe  
Met Ser Thr Ser Val Gly Asp Arg Val Ser  
Ile Thr Cys Lys Ala Ser Gln Asp Val Asn  
Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro  
10 Gly Gln Ser Pro Lys Leu Leu Leu Tyr Ser  
Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp  
His Phe Thr Gly Ser Gly Ser Gly Thr Asp  
Phe Thr Phe Thr Ile Ser Gly Val Gln Ala  
15 Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln  
His Tyr Ser Pro Pro Leu Thr Phe Gly Ala  
Gly Thr Lys Leu Glu Leu Lys .

16. An immunoglobulin L chain variable region fragment having the following amino acid sequence

25 Asp Ile Val Met Thr Gln Ser His Lys Phe  
Met Ser Thr Ser Val Gly Asp Arg Val Thr  
Ile Thr Cys Lys Ala Ser Gln Asp Val Thr  
30 Thr Asp Val Ala Trp Tyr Gln Gln Lys Pro  
Arg Gln Ser Pro Lys Leu Leu Ile Tyr Ser  
Ala Ser Tyr Arg Tyr Thr Gly Val Pro Asp  
Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp  
35 Phe Thr Phe Thr Ile Ser Ser Val Gln Ala  
Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln  
His Tyr Ser Thr Ala Trp Thr Phe Gly Gly  
40 Gly Thr Lys Leu Glu Ile Lys .



17. DNA and RNA fragments each encoding an immunoglobulin L chain variable region fragment which contains a base sequence encoding a hypervariable region CDR1 having an amino acid sequence selected from

5 (1) Tyr Arg Ala Ser Lys Ser Val  
Gln Leu His Leu Ala Ile Val  
Tyr Met His;  
Tyr Arg Ala Ser Lys Ser Val  
10 Ser Thr Ser Gly Tyr Ser Tyr  
Met His;  
Lys Ala Ser Gln Asp Val Asn  
15 Thr Ala Val Ala; and  
Lys Ala Ser Gln Asp Val Thr  
Thr Asp Val Ala ,

20 a base sequence encoding a hypervariable region CDR2 having an amino acid sequence selected from

(2) Leu Val Ser Asn Leu Glu Ser;  
Leu Val Ser Asn Leu Asp Ser; and  
25 Ser Ala Ser Tyr Arg Tyr Thr ,

and a base sequence encoding a hypervariable region CDR3 having an amino acid sequence selected from

30 (3) Gln His Ile Arg Val Ala Tyr  
Thr;  
Gln His Ile Arg Gly Ala Tyr  
35 Thr;  
Gln His Ile Glu Gly Ala Tyr  
Thr;  
Gln Gln His Tyr Ser Pro Pro  
40 Leu Thr; and  
Gln Gln His Tyr Ser Thr Ala  
Trp Thr .

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18. An immunoglobulin L chain variable region fragment having the following base sequence

5 GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC  
TTA GCT GTA TCT CCT CTG GGG CAG AGG GCC  
ACC ATC TCA TAC AGG GCC AGC AAA AGT GTG  
CAG TTA CAT CTG GCT ATA GTT TAT ATG CAC  
10 TGG AAC CAA CAG AAA CCA GGA CAG CCA CCC  
AGA CTC CTC ATC TAT CTT GTA TCC AAC CTA  
GAA TCT GGG GTC CCT GCC AGG TTC AGT GGC  
AGT GGG TCT GGG ACA GAC TTC ACC CTC AAC  
15 ATC CAT CCT GTG GAG GAG GAG GAT GCT GCA  
ACC TAT TAC TGT CAG CAC ATT AGG GTA GCT  
TAC ACG TTC GGA GGG GGG ACC AAG CTG GAA  
20 ATA AAA .

19. An immunoglobulin L chain variable region fragment having the following base sequence

25 GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC  
TTA GCT GTA TCT CTG GGG CAG AGG GCC TCC  
30 ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT  
ACA TCT GGC TAT AGT TAT ATG CAC TGG AAC  
CAA CAG AAA CCA GGA CAG CCA CCC AGA CTC  
CTC ATC TAT CTT GTA TCC AAC CTA GAA TCT  
35 GGG GTC CCT GCC AGG TTC AGT GGC AGT GGG  
TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT  
CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT  
40 TAC TGT CAG CAC ATT AGG GGA GCT TAC ACG  
TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA .

20. An immunoglobulin L chain variable region fragment having the following base sequence

5 GAC ATT GTG CTG ACA CAG TCT CCT GCT TCC  
TTA GCT GTA TCT CTG GGG CAG AGG GCC ACC  
ATC TCA TAC AGG GCC AGC AAA AGT GTC AGT  
ACA TCT GGC TAT AGT TAT ATG CAC TGG AAC  
CAA CAG AGA CCA GGA CAG CCA CCC AGA CTC  
10 CTC ATC TAT CTT GTA TCC AAC CTA GAC TCT  
GGG GTC CCT GCC AGG TTC AGT GGC AGT GGG  
TCT GGG ACA GAC TTC ACC CTC AAC ATC CAT  
CCT GTG GAG GAG GAG GAT GCT GCA ACC TAT  
15 TAC TGT CAG CAC ATT GAG GGA GCT TAC ACG  
TTC GGA GGG GGG ACC AAG CTG GAA ATA AAA .

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21. An immunoglobulin L chain variable region fragment having the following base sequence

25 GAC ATT GTG ATG ACC CAG TCT CAC AAA TTC  
ATG TCC ACA TCA GTA GGA GAC AGG GTC AGT  
ATC ACC TGC AAG GCC AGT CAG GAT GTG AAT  
ACT GCT GTA GCC TGG TAT CAA CAG AAA CCA  
30 GGA CAA TCT CCT AAA CTA CTG CTT TAC TCG  
GCA TCC TAC CGG TAC ACT GGA GTC CCT GAT  
CAC TTC ACT GGC AGT GGA TCT GGG ACG GAT  
TTC ACT TTC ACC ATC AGC GGT GTG CAG GCT  
35 GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA  
CAT TAT AGT CCT CCT CTC ACG TTC GGT GCT  
40 GGG ACC AAG CTG GAA CTG AAA .

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22. An immunoglobulin L chain variable region fragment having the following base sequence

5 GAC ATT GTG ATG ACA CAG TCT CAC AAA TTC  
 ATG TCC ACA TCA GTT GGA GAC AGG GTC ACC  
 ATC ACC TGC AAG GCC AGT CAG GAT GTG ACT  
 ACT GAT GTA GCC TGG TAT CAA CAG AAA CCA  
 10 CGA CAA TCT CCT AAA CTA CTG ATT TAC TCG  
 CCA TCC TAT CGG TAC ACT GGA GTC CCT GAT  
 CGC TTC ACT GGC AGT GGA TCT GGG ACG GAT  
 TTC ACT TTC ACC ATC AGC AGT GTG CAG GCT  
 15 GAA GAC CTG GCA GTT TAT TAC TGT CAG CAA  
 CAT TAT AGT ACT GCG TGG ACG TTC GGT GGT  
 GGC ACC AAG CTG GAA ATC AAA .

23. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 2 and the immunoglobulin L chain variable region fragment according to claim 12.

24. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 2 and the immunoglobulin L chain variable region fragment according to claim 13.

25. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 3 and the immunoglobulin L chain variable region fragment according to claim 14.

26. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 4 and the immunoglobulin L chain variable region fragment according to claim 15.

27. An Fv region fragment comprising the immunoglobulin H chain variable region fragment according to claim 5 and the immunoglobulin L chain variable region fragment according to claim 16.

FIG. 1

Idio 3

Idio 17

Idio 20

Idio 27

Idio 33

+	$\lambda$	K	G3	G2b	G2a	G1	M	A
+	$\lambda$	K	G3	G2b	G2a	G1	M	A
+	$\lambda$	K	G3	G2b	G2a	G1	M	A
+	$\lambda$	K	G3	G2b	G2a	G1	M	A
+	$\lambda$	K	G3	G2b	G2a	G1	M	A

FIG. 2

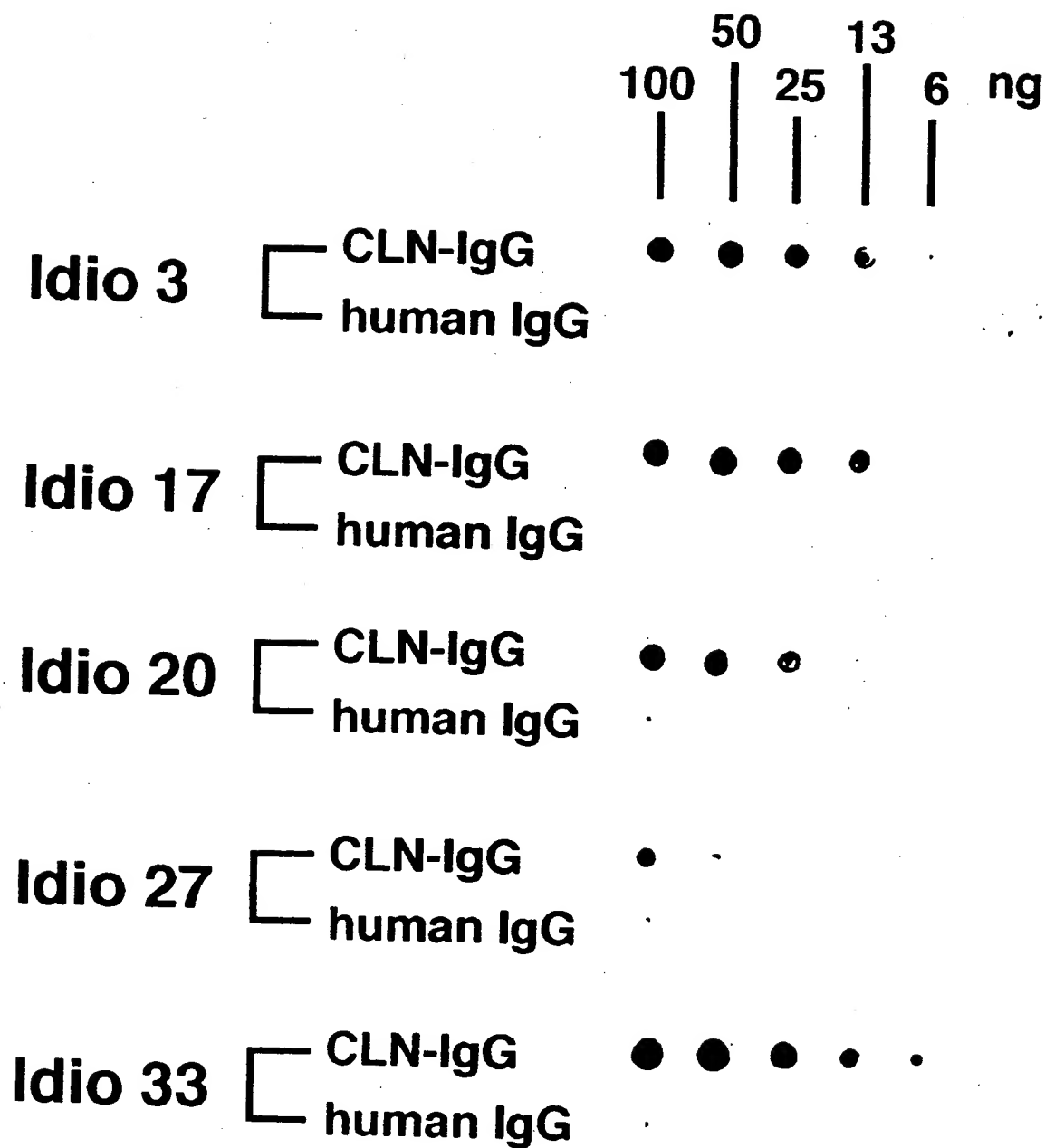


FIG. 3

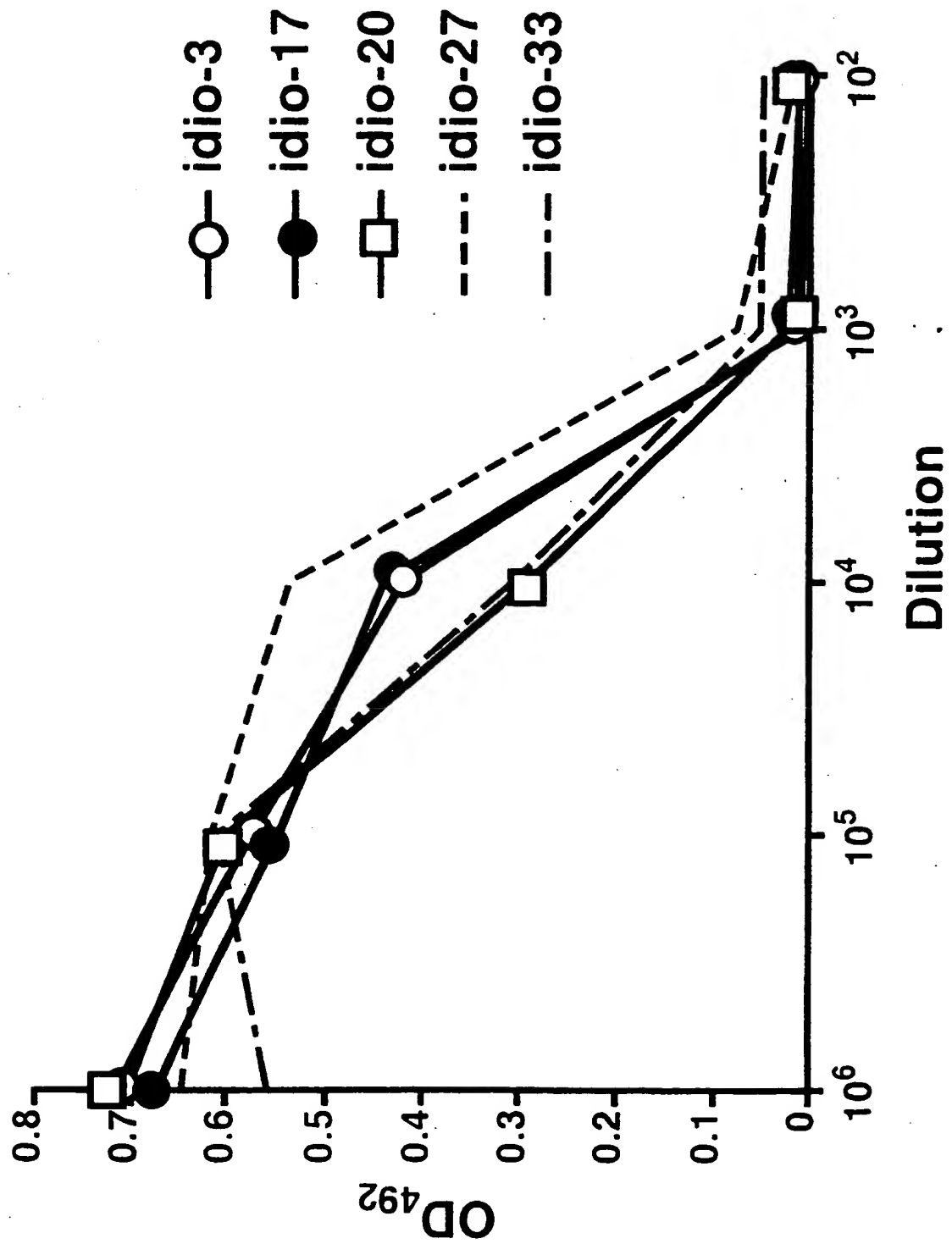


FIG. 4

3 17 20 27 33					
FR 1	1	Glu	Glu	Glu	Glu
	2	Val	Val	Val	Val
	3	Gln	Gln	Lys	Lys
	4	Leu	Leu	Leu	Leu
	5	Gln	Gln	Val	Val
	6	Gln	Gln	Glu	Glu
	7	Ser	Ser	Ser	Ser
	8	Gly	Gly	Gly	Gly
	9	Thr	Thr	Gly	Gly
	10	Val	Val	Gly	Gly
	11	Leu	Leu	Leu	Leu
	12	Ala	Ala	Val	Val
	13	Arg	Arg	Gln	Gln
	14	Pro	Pro	Pro	Pro
	15	Gly	Gly	Gly	Gly
	16	Ala	Ala	Gly	Gly
	17	Ser	Ser	Ser	Ser
	18	Val	Val	Leu	Leu
	19	Lys	Lys	Arg	Arg
	20	Met	Met	Leu	Leu
	21	Ser	Ser	Ser	Ser
	22	Cys	Cys	Cys	Cys
	23	Lys	Lys	Ala	Ala
	24	Ala	Ala	Thr	Thr
	25	Ser	Ser	Ser	Ser
	26	Gly	Gly	Gly	Gly
	27	Tyr	Tyr	Leu	Phe
	28	Thr	Thr	Thr	Thr
	29	Phe	Phe	Phe	Phe
	30	Asn	Asn	Thr	Thr
CDR 1	31	Ser	Ser	Asp	Asn
	32	Tyr	Tyr	Tyr	Tyr
	33	Trp	Trp	Tyr	Trp
	34	Met	Met	Met	Met
FR 2	35	His	His	Asn	Asn
	36	Trp	Trp	Trp	Trp
	37	Val	Val	Val	Val
	38	Lys	Lys	Arg	Arg
	39	Gln	Gln	Gln	Gln
	40	Arg	Arg	Pro	Pro
	41	Pro	Pro	Pro	Pro
	42	Gly	Gly	Gly	Gly
	43	Gln	Gln	Lys	Lys
	44	Gly	Gly	Glu	Ala
	45	Leu	Leu	Leu	Leu
	46	Glu	Glu	Glu	Glu
	47	Trp	Trp	Trp	Trp
	48	Ile	Ile	Leu	Ile
CDR 2	49	Gly	Gly	Gly	Gly
	50	Ala	Ala	Phe	Phe
	51	Ile	Ile	Ile	Ile
	52	Tyr	Tyr	Arg	Arg
	52A	Pro	Pro	Asn	Asn
	52B	---	---	Lys	Lys
	52C	---	---	Ala	Ala
	53	Gly	Gly	Asn	Asn
	54	Asn	Asn	Leu	Tyr
	55	Ser	Ser	Tyr	Tyr
	56	Asp	Asp	Thr	Thr
	57	Ile	Ile	Thr	Thr
	58	Ser	Ser	Asp	Glu
	59	Tyr	Tyr	Tyr	Tyr
	60	Ser	Ser	Ser	Ser
	61	Gln	Gln	Ala	Ala
	62	Asn	Asn	Ser	Ser
	63	Phe	Phe	Val	Val
	64	Lys	Lys	Lys	Lys
	65	Asp	Asp	Gly	Gly
	66	Arg	Arg	Arg	Arg
	67	Ala	Ala	Phe	Phe
FR 3	68	Lys	Lys	Thr	Thr
	69	Leu	Leu	Ile	Ile
	70	Thr	Thr	Ser	Ser
	71	Ala	Ala	Arg	Arg
	72	Val	Val	Asp	Asp
	73	Thr	Thr	Asn	Asn
	74	Ser	Ser	Pro	Ser
	75	Thr	Thr	Gln	Gln
	76	Ser	Ser	Ser	Ser
	77	Thr	Thr	Ile	Ile
	78	Ala	Ala	Leu	Leu
	79	Tyr	Tyr	Tyr	Tyr
	80	Met	Met	Leu	Leu
	81	Glu	Glu	Gln	Gln
	82	Leu	Leu	Met	Met
	82A	Arg	Arg	Asn	Asn
	82B	Ser	Ser	Thr	Thr
	82C	Leu	Leu	Leu	Leu
	83	Thr	Thr	Thr	Thr
	84	Asn	Asn	Thr	Ala
	85	Glu	Glu	Glu	Glu
	86	Asp	Asp	Asp	Asp
	87	Ser	Ser	Ser	Ser
	88	Ala	Ala	Ala	Ala
	89	Val	Val	Thr	Thr
	90	Tyr	Tyr	Tyr	Tyr
	91	Phe	Phe	Tyr	Tyr
	92	Cys	Cys	Cys	Cys
	93	Thr	Thr	Ala	Ala
	94	Lys	Lys	Arg	Arg
3RDC	95	Glu	Glu	Asp	Asp
	96	Glu	Glu	Arg	Gly
	97	Tyr	Tyr	Gly	Phe
	98	Asp	Asp	Gly	Leu
	99	Tyr	Tyr	Arg	Arg
	100	Asp	Asp	Asp	Asp
	100A	Thr	Thr	---	---
	100B	---	---	---	---
	100C	---	---	---	---
	100D	---	---	---	---
FR 4	100E	---	---	---	---
	100F	---	---	---	---
	100G	---	---	---	---
	100H	---	---	---	---
	100I	---	---	Trp	Trp
	100J	---	---	Tyr	Tyr
	100K	Leu	Leu	Phe	Phe
	101	Asp	Asp	Asp	Asp
	102	Tyr	Tyr	Val	Val
	103	Trp	Trp	Trp	Trp
	104	Gly	Gly	Gly	Gly
	105	Gln	Gln	Ala	Ala
	106	Gly	Gly	Gly	Gly
	107	Thr	Thr	Thr	Thr
	108	Ser	Ser	Thr	Thr
	109	Val	Val	Val	Val
	110	Thr	Thr	Thr	Thr
	111	Val	Val	Val	Val
	112	Ser	Ser	Ser	Ser
	113	Ser	Ser	Ser	Ala



FIG. 5

3 17 20 27 33

F R 1	1	Asp	Asp	Asp	Asp	Asp
	2	Ile	Ile	Ile	Ile	Ile
	3	Val	Val	Val	Val	Val
	4	Leu	Leu	Leu	Met	Met
	5	Thr	Thr	Thr	Thr	Thr
	6	Gln	Gln	Gln	Gln	Gln
	7	Ser	Ser	Ser	Ser	Ser
	8	Pro	Pro	Pro	His	His
	9	Ala	Ala	Ala	Lys	Lys
	10	Ser	Ser	Ser	Phe	Phe
	11	Leu	Leu	Leu	Met	Met
	12	Ala	Ala	Ala	Ser	Ser
	13	Val	Val	Val	Thr	Thr
	14	Ser	Ser	Ser	Ser	Ser
	15	Pro	Leu	Leu	Val	Val
	16	Leu	Gly	Gly	Gly	Gly
	17	Gly	Gln	Gln	Asp	Asp
	18	Gln	Arg	Arg	Arg	Arg
	19	Arg	Ala	Ala	Val	Val
	20	Ala	Ser	Thr	Ser	Thr
	21	Thr	Ile	Ile	Ile	Ile
	22	Ile	Ser	Ser	Thr	Thr
	23	Ser	---	---	Cys	Cys
C D R 1	24	Tyr	Tyr	Tyr	Lys	Lys
	25	Arg	Arg	Arg	Ala	Ala
	26	Ala	Ala	Ala	Ser	Ser
	27	Ser	Ser	Ser	Gln	Gln
	27A	Lys	Lys	Lys	---	---
	27B	Ser	Ser	Ser	---	---
	27C	Val	Val	Val	---	---
	27D	Gln	Ser	Ser	---	---
	27E	Leu	Thr	Thr	---	---
	27F	His	---	---	---	---
	28	Leu	Ser	Ser	Asp	Asp
	29	Ala	Gly	Gly	Val	Val
F R 2	30	Ile	Tyr	Tyr	Asn	Thr
	31	Val	Ser	Ser	Thr	Thr
	32	Tyr	Tyr	Tyr	Ala	Asp
	33	Met	Met	Met	Val	Val
	34	His	His	His	Ala	Ala
	35	Trp	Trp	Trp	Trp	Trp
	36	Asn	Asn	Asn	Tyr	Tyr
	37	Gln	Gln	Gln	Gln	Gln
	38	Gln	Gln	Gln	Gln	Gln
	39	Lys	Lys	Arg	Lys	Lys
	40	Pro	Pro	Pro	Pro	Pro
	41	Gly	Gly	Gly	Gly	Arg
C D R 2	42	Gln	Gln	Gln	Gln	Gln
	43	Pro	Pro	Pro	Ser	Ser
	44	Pro	Pro	Pro	Pro	Pro
	45	Arg	Arg	Arg	Lys	Lys
	46	Leu	Leu	Leu	Leu	Leu
	47	Leu	Leu	Leu	Leu	Leu
	48	Ile	Ile	Ile	Leu	Ile
	49	Tyr	Tyr	Tyr	Tyr	Tyr
	50	Leu	Leu	Leu	Ser	Ser
	51	Val	Val	Val	Ala	Ala
	52	Ser	Ser	Ser	Ser	Ser
	53	Asn	Asn	Asn	Tyr	Tyr
	54	Leu	Leu	Leu	Arg	Arg
	55	Glu	Glu	Asp	Tyr	Tyr
	56	Ser	Ser	Ser	Thr	Thr
	57	Gly	Gly	Gly	Gly	Gly
	58	Val	Val	Val	Val	Val
	59	Pro	Pro	Pro	Pro	Pro
	60	Ala	Ala	Ala	Asp	Asp
	61	Arg	Arg	Arg	His	Arg
	62	Phe	Phe	Phe	Phe	Phe
	63	Ser	Ser	Ser	Thr	Thr
	64	Gly	Gly	Gly	Gly	Gly

F R 3	65	Ser	Ser	Ser	Ser	Ser
	66	Gly	Gly	Gly	Gly	Gly
	67	Gly	Ser	Ser	Ser	Ser
	68	Gly	Gly	Gly	Gly	Gly
	69	Thr	Thr	Thr	Thr	Thr
	70	Asp	Asp	Asp	Asp	Asp
	71	Phe	Phe	Phe	Phe	Phe
	72	Thr	Thr	Thr	Thr	Thr
	73	Leu	Leu	Leu	Phe	Phe
	74	Asn	Asn	Asn	Thr	Thr
	75	Ile	Ile	Ile	Ile	Ile
	76	His	His	His	Ser	Ser
	77	Pro	Pro	Pro	Ser	Ser
	78	Val	Val	Val	Val	Val
	79	Glu	Glu	Glu	Gln	Gln
	80	Glu	Glu	Glu	Ala	Ala
	81	Glu	Glu	Glu	Glu	Glu
	82	Asp	Asp	Asp	Asp	Asp
	83	Ala	Ala	Ala	Leu	Leu
	84	Ala	Ala	Ala	Ala	Ala
	85	Thr	Thr	Thr	Val	Val
	86	Tyr	Tyr	Tyr	Tyr	Tyr
	87	Tyr	Tyr	Tyr	Tyr	Tyr
	88	Cys	Cys	Cys	Cys	Cys
C D R 3	89	Gln	Gln	Gln	Gln	Gln
	90	His	His	His	Gln	Gln
	91	Ile	Ile	Ile	His	His
	92	Arg	Arg	Glu	Tyr	Tyr
	93	Val	Gly	Gly	Ser	Ser
	94	Ala	Ala	Ala	Pro	Thr
	95	---	---	---	Pro	Ala
	95A	---	---	---	---	---
	95B	---	---	---	---	---
	95C	---	---	---	---	---
	95D	---	---	---	---	---
	95E	---	---	---	---	---
F R 4	95F	---	---	---	---	---
	96	Tyr	Tyr	Tyr	Leu	Trp
	97	Thr	Thr	Thr	Thr	Thr
	98	Phe	Phe	Phe	Phe	Phe
	99	Gly	Gly	Gly	Gly	Gly
	100	Gly	Gly	Gly	Ala	Gly
	101	Gly	Gly	Gly	Gly	Gly
	102	Thr	Thr	Thr	Thr	Thr
	103	Lys	Lys	Lys	Lys	Lys
	104	Leu	Leu	Leu	Leu	Leu
	105	Glu	Glu	Glu	Glu	Glu
	106	Ile	Ile	Ile	Leu	Ile
	106A	---	---	---	---	---
	107	Lys	Lys	Lys	Lys	Lys



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# EUROPEAN SEARCH REPORT

Application Number  
EP 94 11 5683

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
A	US-A-5 208 146 (R. ERIE) * the whole document *	1-27	C12N15/13 C07K16/42
A	WO-A-89 00050 (AKZO NV) * claims * * examples *	1-27	
A	WO-A-93 10221 (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA) * the whole document *	1-27	
A	EUROPEAN JOURNAL OF CANCER AND CLINICAL ONCOLOGY, vol.24, no.5, May 1988, OXFORD, GB pages 829 - 838 Y. AOTSUKA ET AL. 'Identification of a malignant cell associated antigen recognized by a human monoclonal antibody.' * abstract *	1-27	
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The present search report has been drawn up for all claims			
Place of search <b>THE HAGUE</b>		Date of completion of the search <b>16 March 1995</b>	Examiner <b>Nooij, F</b>
<b>CATEGORY OF CITED DOCUMENTS</b> X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

EPO FORM 1503 03.82 (P04C01)



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# EUROPEAN SEARCH REPORT

Application Number  
EP 94 11 5683

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
A	CANCER RESEARCH, vol.52, no.9, 1 May 1992, PHILADELPHIA PA, USA pages 2603 - 2609 W. TADDEI-PETERS ET AL. 'Quantitation of human tumor-reactive monoclonal antibody 16.88 in the circulation and localization of 16.88 in colorectal metastatic tumor tissue using murine antiidiotypic antibodies.' * abstract *	1-27	
P,A	MOLECULAR IMMUNOLOGY, vol.30, no.16, November 1993, OXFORD, GB pages 1481 - 1489 K. YAGO ET AL. 'Immunoglobulin variable region sequences of two human monoclonal antibodies directed to an onco-developmental carbohydrate antigen, lactotetraosylceramide (LcOse4Cer).' * abstract *	1-27	
The present search report has been drawn up for all claims			TECHNICAL FIELDS SEARCHED (Int.Cl.6)
Place of search THE HAGUE		Date of completion of the search 16 March 1995	Examiner Nooij, F
<p><b>CATEGORY OF CITED DOCUMENTS</b></p> <p>X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document</p> <p>T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons</p> <p>&amp; : member of the same patent family, corresponding document</p>			

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